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CONTENTS.

	PAGE.
A Case of Combined Protozoan and Bacterial Infection. By Simon Flexner, M. D.,	171
Notes on Two Cases of Ureteral Abnormality. By George Blumer, M. D.,	174
Tumors in the Mouse. By L. E. Livingood, M. D.,	177
The Anatomical Changes in Two Cases of Retinal Detachment. By Robert L. Randolph, M. D.,	179
The Bubonic Plague. By Simon Flexner, M. D.,	181
Absolute Alcohol as a Disinfectant for Instruments. A Bacteriological Study. By Robert L. Randolph, M. D.,	185
Proceedings of Societies: Hospital Medical Society,	188
Generalized Melanotic Sarcoma [Dr. Blumer];—Specimen of Adeno-Carcinoma of Pancreas [Dr. Blumer].	
Notes on New Books,	190
Special Courses for Graduates in Medicine. Change of Date,	192

A CASE OF COMBINED PROTOZOAN AND BACTERIAL INFECTION.

AMŒBIC DYSENTERY, MALARIA, AND MICROCOCCUS LANCEOLATUS, ACUTE FIBRINO-PURULENT PERITONITIS.

By Simon Flexner, M. D., *Associate Professor of Pathology, Johns Hopkins University; Resident Pathologist, Johns Hopkins Hospital.*

[*From the Pathological Laboratory of the Johns Hopkins University and Hospital.*]

The recent literature upon malarial infections in human beings contains a few instances of associated protozoan and of mixed protozoan and bacterial infections. Among the associated protozoan infections may be included cases of multiple malarial infections, in which an individual may be infected at the same time with different groups or generations of the same organisms, or of organisms of different types, and the rare co-existence of malarial and other protozoan infections, such as amœbic dysentery.* The instances of mixed protozoan and bacterial infection are more numerous and embrace the combination of pneumonia (lobar and lobular) and malaria, bronchitis and malaria, and the rarer one of typhoid fever and malaria. Respecting the cases of concurrent pneumonia and malaria, it may be said that the same bacteria as are concerned with the causation of uncomplicated cases of this disease are found in the lungs in the mixed infections. Barker has described a case of associated erysipelas and tertian malaria in which an invasion of the blood with streptococci existed, both micro-organisms appearing there and in the internal organs in large numbers.

The present case obtains its interest in part from the unusual character of the infection, and in part from the extent, character and consequences of the intestinal lesions. Dr. Thayer has kindly supplied the following notes of the clinical history:

The patient, A. J., was a Pole about 29 years of age, from whom a satisfactory history could not be obtained. He had been living in a malarious district since March of the past year (1895), but he had been quite well until three weeks prior to his entrance, which was on October 21st. His illness began with diarrhœa, which rapidly assumed a severe character, the movements containing much blood and mucus. During these three weeks he stated that he had several times experienced slight chilly sensations and also felt feverish. On entrance to the hospital he was very anæmic, extremely sallow; had a palpable spleen, slight fever and severe dysentery, the movements showing much blood and mucus. The dejections contained many motile amœbæ having the characteristic appearances of the amœba coli. The blood examinations showed hyaline bodies and crescentic and ovoid pigmented forms of

*Cf. Thayer and Hewetson: The Malarial Fevers of Baltimore. Johns Hopkins Hospital Reports, 1895, vol. V. Barker: A Study of Some Fatal Cases of Malaria, *idem*, alludes to a case of combined malaria and amœbic dysentery occurring in the hospital.

the malarial parasite. Under the administration of five grain doses of quinine every three hours the temperature fell. The diarrhœa was treated with irrigations of quinine ($\frac{1}{1500}$) repeated twice daily, but without apparent effect. The patient continued to lose blood per rectum and died on the 2nd of November.

The *autopsy* was performed 7 hours post mortem. Body of a moderately strongly built, much emaciated man. The surface presented a distinctly sallow hue. The mucous membranes of the mouth and conjunctivæ were extremely pale. The abdomen was moderately distended; the subcutaneous fat almost absent; the muscles dark-brownish red in color.

The peritoneal cavity. The omentum was well spread out, covering the intestines, but it presented an opaque appearance and was covered with a sticky exudate. The loops of the moderately distended small intestine were glued together by a similar sticky exudate. The serous membrane itself was in places vividly injected. In the fossæ small accumulations of fluid containing flakes of fibrin were encountered. The omentum was adherent along its lower border to the much enlarged and inflamed appendix vermiformis. The appendix lay anterior to the cæcum and between it and the anterior abdominal wall; it was provided with a mesentery which reached within 3 cm. of its tip, and at the termination of this the appendix was bent sharply upon itself, giving rise to a right angle. The distal 3 cm. of appendix was the least dilated part; the remainder had the thickness of the index finger and presented in addition three bulbous enlargements, which on section were found to correspond to areas of necrotic tissue. The whole was embedded in a sticky, opaque exudate.

Intestines. The large intestines were greatly distended. The sigmoid flexure was of rigid consistence and projected beyond the pelvic brim. Within this portion for a distance of 2x5 cm. the serous coat was infiltrated with blood and presented a necrotic appearance. On opening the large intestine the entire mucous membrane was found in a frayed and sloughing condition, opaque, everywhere infiltrated with gelatinous pus, and evidently necrotic. The necrosis seemed to extend far beyond the mucous coat and to involve the deeper layers. The walls, as a whole, were much thickened. In many places coagula of blood were discovered. Amid this general necrosis and sloughing more circumscribed ulcerations existed, some of which seemed to reach to the peritoneal coat. These in particular were surrounded by thickened and purulent margins, and at times they definitely undermined the adjacent tissues. The ulcerations and sloughing extended from the rectum to the cæcum, involving the whole of the latter, penetrating into the appendix, but ending abruptly with the ileocæcal valve. The small intestine was entirely free from ulceration, and it showed throughout nearly its whole extent, although most prominently upon the crests of the valvulæ conniventes, a slaty pigmentation. The duodenum was more pigmented than other parts of the small intestine.

The *spleen* was enlarged, weighed 380 grams, its capsule was wrinkled, and on section it presented a bluish black color. In consistence it was almost diffluent. The Malpighian bodies appeared enlarged, the pulp increased.

The *liver* weighed 2100 grams, its color was dark and slaty. Small greyish white nodules could be seen on section, which varied in size from a pin point to a hemp seed. The larger ones could easily be made out to be abscesses, the contents of which were opaque, gelatinous and pus-like. The wall of the *gall bladder* was thickened and infiltrated with a similar exudate to that covering the peritoneum. The mucous membrane was, however, intact. The remainder of the organs exhibited no remarkable lesions.

Microscopical examination of the fresh specimen. Attention was first directed to the study of the exudates for amœbæ, and for this purpose pus (*a*) from the peritoneal cavity, (*b*) from the intestinal contents, (*c*) from the liver abscesses, was employed. The most painstaking search failed to reveal amœbæ in the pus from the peritoneal cavity, while on the other hand many typical living and moving amœbæ were discovered in the pus from the ulcers in the large intestine and the intestinal contents, and a smaller number in the contents of the liver abscesses.

The exclusion of amœbæ from the peritoneal exudate led next to the staining of cover-slips for bacteria. By the use of ordinary staining agents (gentian violet, methylene blue) myriads of capsulated diplococci resembling the micrococcus lanceolatus were revealed. The contents of the liver abscesses, stained in the same manner, failed to show any bacteria whatever. The microscopical examination of the abscess contents indicated that fewer pus cells and more necrotic and disintegrating liver cells composed these than in ordinary abscesses, thus recalling the fact pointed out by Councilman and Lafleur* in their monograph on amœbic dysentery, that true suppuration is not caused by the amœba dysenteriæ.

The source of the bacteria found in the peritoneal exudate, and which evidently were the cause of the acute peritonitis, was sought in the intestinal contents, where, as is well known, they are not infrequently contained, and from which source, as we have previously pointed out,† they may invade the peritoneum and set up a fatal peritonitis. The condition of the appendix vermiformis, which arrested attention from its swollen and necrotic appearance, was believed to have led to the escape of the micro-organisms in question. Upon closer examination it was found that corresponding with the dilatations previously described, the entire wall was in a necrotic condition. The ulcerations themselves reached deeply into the inner coats, but did not penetrate all the coats. The lumen of the swollen appendix was filled with yellow, gelatinous pus quite resembling that found in the peritoneal cavity itself. Cover-slip preparations showed many encapsulated diplococci, besides several kinds of bacilli. The former much predominated in numbers.

Malarial bodies were not numerous in smear preparations from the organs, although pigment was abundant. However, a few undoubted ovoid bodies were found in the smears from the spleen and bone marrow.

Cultures. Petri's plates were made from the blood in the heart, the exudates and all the organs, upon agar-agar. Those from the *heart's blood*, *spleen*, *lungs*, and *liver abscesses* showed

*Johns Hopkins Hospital Reports, vol. II, 1891, p. 395.

†Johns Hopkins Hospital Bulletin, 1895, No. 49, p. 64.

no growth after having been kept at the temperature of the thermostat for 48 hours.

Peritoneum. The plate was crowded with colonies, apparently of two kinds, which, owing to the large numbers, probably did not reach full development. The larger colonies consisted of bacilli which were identified and shown to be the bacillus coli communis. The smaller colonies (predominating) were made up of oval diplococci which were shown (cultures and animal experiments) to be the micrococcus lanceolatus. The plate made from the *bile* contained 7, from the *liver* 30 colonies of the bacillus coli communis. The plate from the *kidney* was crowded with colonies of the colon bacillus, among which a few smaller colonies of diplococci were found, these being the micrococcus lanceolatus.

Histological examination. The microscopical examination of the hardened tissues was confirmatory only of the features of the case as already described. Nothing new was discovered. As regards the malarial pigmentation, the dark pigment was found especially in the liver and spleen (bone-marrow not studied), and in these organs in the usual situations The parasites themselves were very difficult of demonstration. The lesions in the large intestine caused by the invasion of the amœbæ were perhaps the most interesting. The necrosis, it was found, extended into, but for the most part not through the innermost muscular tunic, but it was surprising to what extent the mucous membrane might be dissected away from the submucosa without losing its vitality. Not a small part of the frayed appearance presented by the large intestine was produced by this partial dissection of the mucous coat. The bases of the ulcers proper were formed for the most part by the circular muscle, which was itself infiltrated with inflammatory products, cells, serum, fibrin. The inflammatory infiltration extended into the depths of the tissue, often to the serous coat, and spread laterally for a great distance. It seems probable that the ulcers in the appendix originally were caused by amœbæ, and that subsequently the extension of the necrosis to the serous surface was the work of the micrococcus lanceolatus.

Amœbæ apparently were abundant. But just here it is proper to state that in the hardened tissues it would be easy to be led into error in regard to the significance of many of the amœba-like cells present. From a study of the transitions of connective-tissue cells and their progeny in the chronically inflamed parts, it is quite certain that many of the bodies resembling amœbæ are swollen and degenerated (fatty or vacuolated) tissue cells. These, too, often lay in definite spaces, and they were found in the submucosa and muscle and within small veins. Without the proof supplied by the examination of the intestinal contents during life and at the autopsy, one must have remained in doubt as to the presence of amœbæ among these elements.

The kidneys showed a moderate degree of parenchymatous degeneration. In addition to this, emboli of liver cells were detected in branches of the renal vein. Similar emboli were discovered in the central veins of the liver lobules not infrequently. Lubarsch* has reviewed the literature upon the subject of "parenchymcell emboli." It appears that liver cell emboli are either of traumatic or of infectious (or due to intoxication) origin. There is no definite relation between the extent of the injury and the occurrence of such emboli. The transported liver cells, besides being found in the veins of the liver, occur in the heart, pulmonary arteries and branches of the renal and hepatic arteries. Among the infectious diseases liver cell emboli are found very often in eclampsia and chorea. In eclampsia they are found in the arteries of the lungs and brain and in the renal veins; in chorea in the hepatic artery and branches of the portal vein (patent foramen ovale). Where hemorrhage, necrosis and softening exist, liver cell emboli are encountered. Thus they have been found in scarlet fever, in softening of hepatic gummata and in liver abscess. The transported liver cells have been followed from the hepatic veins into the coronary, renal and other arteries. Their occurrence in veins—renal and cerebral—is attributed to retrograde embolism, for which a high degree of venous stasis, such as occurs in eclampsia, has been assumed. Evidence of such stagnation is wanting in our case. On the other hand the disintegration of liver tissue, such as has been found in other cases, is supplied by the abscess formation and circumscribed necrosis in the liver. Lubarsch states that the conveyed liver cells may persist from 3 weeks to 2½ months, but evidences of proliferation have never been observed.

Remarks by Dr. BARKER: The case is an interesting one on account of the curious combination of infections. In studying the fatal cases of malaria from Professor Osler's wards my attention was called to the fact that bacterial infections were often concurrent with malarial infections. In one instance a double protozoa infection had been noted, and since that study was made several such double protozoan infections have been observed in the hospital. This case is the first one in which we have to deal with a double protozoan infection associated with a bacterial infection.

* Fortschritte der Medizin, Band XI, 1893.

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NOTES ON TWO CASES OF URETERAL ABNORMALITY.

By George Blumer, M. D., *Assistant in Pathology, Johns Hopkins University.*

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The following two cases of ureteral anomaly, which have recently come under observation, seem uncommon enough to merit description. Through the kindness of Dr. Kelly we are enabled to supplement the descriptions by plates.

The clinical histories of the cases have no special bearing upon the pathological findings, with the exception of the fact that in case No. 1 an attack of acute cystitis had occurred some five years before death; the notes are therefore confined to the pathological aspects of the cases.

Case 1.—*Anatomical Diagnosis.* Diphtheritic inflammation of the bladder, left ureter, and left renal pelvis; suppurative nephritis and perinephritis of the left kidney; hydro-ureter and hydro-nephrosis of the right kidney; miliary abscesses in the right kidney; prolapse of the ureteral and bladder mucous membrane into the bladder cavity; localized fibrinous peritonitis; acute bronchitis; fatty degeneration and cloudy swelling of the liver; slight general arterio-sclerosis.

The following is the abstract from the autopsy protocol referring to the ureters and bladder:

The right ureter is dilated to the size of a lead pencil, and contains pale, cloudy urine. The walls are thin. The mucous membrane is congested. There is nowhere any constriction until the bladder is reached.

The left ureter is dilated to about the size of the normal ileum, its walls are markedly thickened, and it contains a thick greenish black purulent material with an offensive odor. The mucous membrane has a dirty, sloughy appearance and a green-black color, its surface shows numerous irregularities in the form of patches of grayish white false membrane formation, the membrane being firmly attached to the subjacent tissue.

The bladder is somewhat enlarged and contains turbid, foul-smelling urine. Its walls are greatly thickened, measuring as much as three centimeters in their thickest part. The mucous membrane is corrugated and of a greenish black color, and shows numerous areas of densely adherent grayish false membrane similar to those seen in the ureter. Projecting into the bladder from a point where the left ureteral orifice is normally present is a pyramidal sac, tense and fluctuating, and evidently containing fluid. This sac hangs free in the cavity of the bladder and reaches from its place of origin nearly to the internal urethral orifice. It is about eight centimeters in length, has a narrow neck, measuring three centimeters in diameter where it joins the bladder wall, and gradually expands as it passes out from this point, reaching its greatest diameter of nine centimeters a short distance from its free end. On its inner side, about its middle, a minute opening can be made out. This opening is circular and just about large enough to admit a pin point; it is situated in the center of a small area of dense fibrous tissue, and is evidently the lower opening of the left ureter. On opening the sac it is found to contain a thick greenish black purulent material similar to that already seen in the left ureter, and the index finger can be passed directly from the sac into the dilated ureter. Both the internal and external surfaces of the sac are covered with mucous membrane which shows patches of false membrane formation similar to those seen in the ureter and bladder. The sac wall appears to be of the same thickness throughout.

From the normal site of the right lower ureteral orifice there projects a similar but much smaller sac three centimeters in length; it is not nearly so tense as the one on the other side. On the inner side of this second sac is an opening the size of a pin's head, from which urine escapes; there is apparently no cicatricial tissue about this opening. The sac communicates freely with the left ureter. The prostate gland is slightly enlarged, but not sufficiently so to offer any obstruction to the outflow of urine.

The urethra is free from obstruction throughout its entire course. A microscopical examination of the sac wall shows that between the two layers of mucous membrane lies connective tissue containing many bundles of unstriped muscle fiber.

Remarks. This peculiar prolapse of the mucous membrane of the lower end of the ureter and that of the adjacent part of the bladder is not of common occurrence, although we find some similar cases on record.

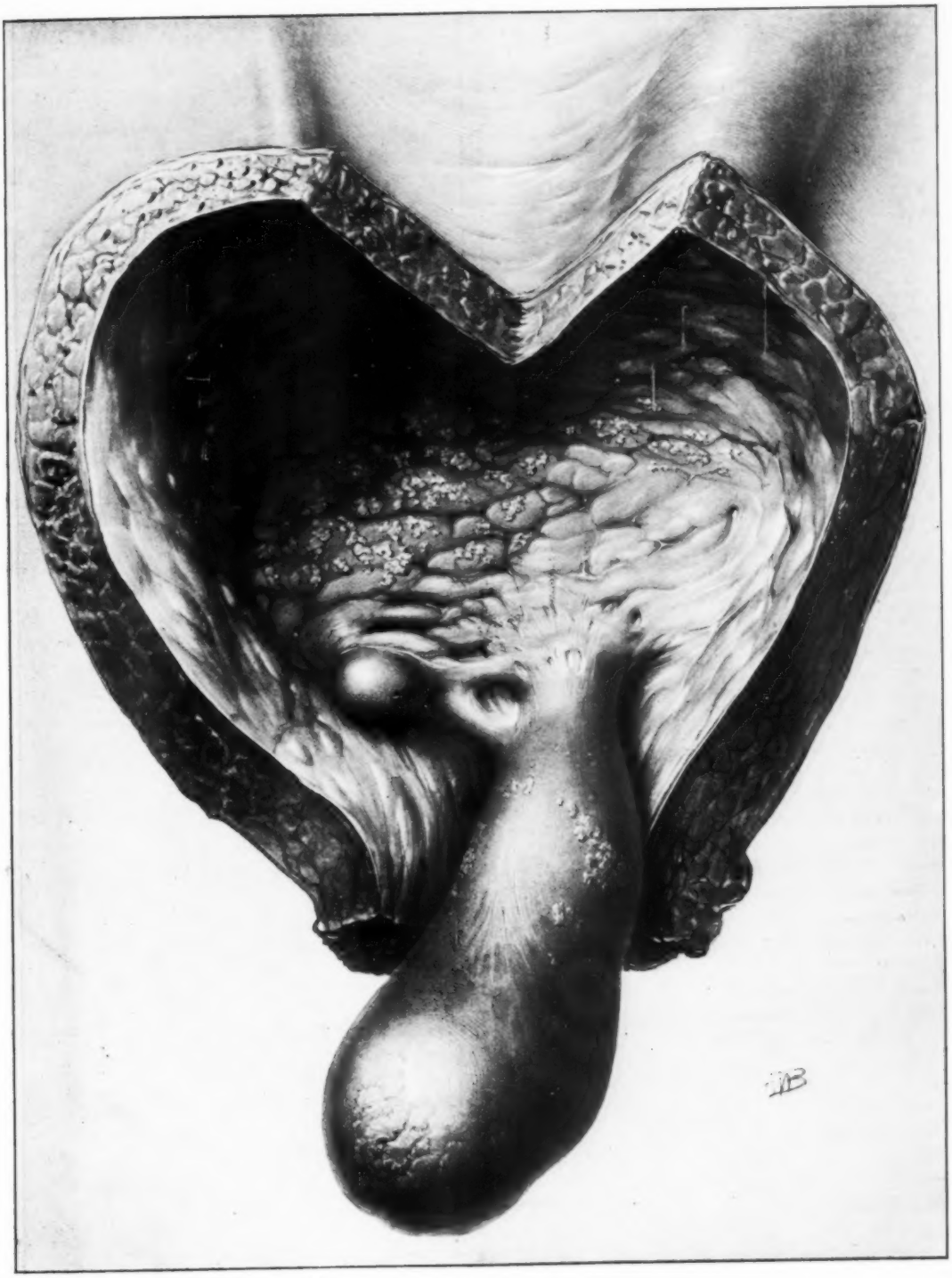
All of these cases seem to come under two main categories:

1. Those cases in which there is distinct evidence that the condition is due to congenital deformity.

2. Those cases in which the process has apparently resulted from some acquired abnormality of the genito-urinary tract. By far the larger number of cases present distinct evidence of congenital malformation; in fact, out of the thirteen cases which we have been able to collect, ten were evidently of congenital origin, death occurring in five of these in the early years of childhood.

All of these five cases occurred in female children, and in four of them, those of Davies-Colley, Caillé, Beach, and Geerdts, there was not only a prolapse into the bladder, but the prolapsed sac actually passed through the urethra and appeared externally.

In the congenital cases proving fatal at a later date, the deformity was in some instances less severe than in the cases ending fatally in early life; in other instances the deformity was just as great in the late as in the early cases, the previous escape of the individual perhaps being due to the fact that he had escaped genito-urinary infection, which seemed to have been the cause of death in the majority of the cases which succumbed early in life. The deformity in these congenital cases consisted in most instances of a partial or complete closure of the lower ureteral orifice. In one case another form of deformity is cited, viz. a ureter having a long portion of its course in the bladder wall, and for this reason sub-



CASE I.

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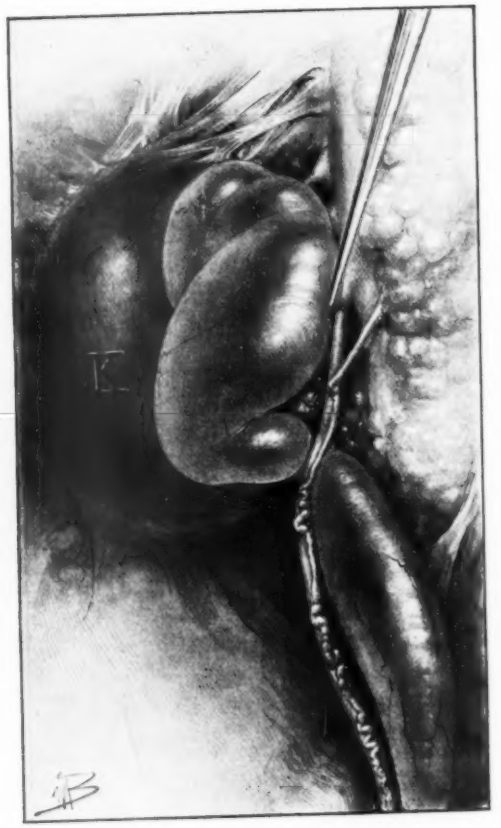

CASE II.

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jected to an abnormal amount of pressure from the bladder musculature.

Accompanying the deformity which was the actual cause of the condition, were often other evidences of congenital malformation. In several instances abnormalities of the kidney pelvis or double ureters were present, and one case is cited in which a deformity of the uterus was noted.

Of the cases in which there was no apparent congenital cause for the condition—and to this class we consider our case belongs—we could find but two examples, one reported by T. Smith, the other by Hutinel.

Smith's case, judging from his description and from an excellent plate which illustrates his article, was almost exactly similar to our own. In his case, however, urinary calculi were present on the right side in the prolapsed pouch, and on the left in the renal pelvis.

In Hutinel's case, which occurred in an old man, the subject of cystitis, the pouching only involved the left ureter. At the time of death the lower orifice of the left ureter was not blocked, as the pouch communicated with the bladder by a pouch the size of a three-franc piece, but there was evidence of a former blocking in a much atrophied kidney on the affected side. Unfortunately Hutinel does not state whether the abnormally large opening which existed between the sac and the bladder was apparently due to simple dilatation or to an ulcerative process.

Judging from the fact that in our case the abnormally small ureteral opening was contained in an area of cicatricial tissue, and from the history that the patient gave of a previous attack of acute cystitis, we are inclined to think that the blocking of the lower ureteral opening was due to an old inflammatory process with a subsequent formation of new tissue, which, in contracting, narrowed the ureteral orifice. It would seem likely that in the cases of Smith and Hutinel the same process might have taken place, as both patients showed evidence of old inflammatory disease of the genito-urinary tract.

As far as the mechanism of the pouching is concerned the cases can again be divided into two classes, those in which there is a uniform dilatation from the pelvis of the kidney down to the end of the sac, and those in which the pelvis of the kidney and the main portion of the ureter are not dilated, the sacculation occurring only at the extreme lower end of the ureter.

In the former class of cases, to which ours belongs, the pouching can be explained by a theory, the essence of which was advanced by Smith in reporting his case. He suggests that the prolapse in these cases is due to the disproportion between the capacity of the ureter and kidney pelvis on the one hand, and the size of the lower ureteral orifice on the other. When, either from an extreme hydro-nephrosis or from an abnormal narrowing of the lower ureteral orifice, the urine is no longer able to escape from this orifice as fast as it is secreted, the distended ureter and kidney pelvis are compressed by the action of the abdominal muscles, particularly during urination and defecation, and a considerable downward pressure is brought to bear on the lower ureteral orifice. This finally results in the prolapse of its mucous membrane, and as the mucous membrane of the bladder is directly continuous with that of the ureter, it is of course pushed downward at the same time, the result being a pouch covered on both sides by mucous membrane, and directly continuous with the dilated ureter and kidney pelvis.

In the cases in which no hydro-nephrosis or hydro-ureter exists—and most of the congenital cases are of this kind—we must seek for some further abnormality in connection with the lower end of the ureter.

According to Boström, this abnormality consists in the manner in which the ureter passes through the bladder wall.

In the normal condition, this author states, the ureters pass obliquely through the bladder wall, and their lower openings lie partly in the bladder musculature, the contraction of the muscle counteracting the downward pressure of the urine and hindering dilatation of the portion of the ureter lying within the musculature.

In the cases in which sacculation takes place the ureter is stated to pass straight through the bladder wall and to end just beneath the mucous membrane, in those cases where the ending is blind. From this it results, according to Boström, that the area of ureter surrounded by muscle is much smaller than normal, the resistance to the downward pressure of the urine is insufficient, and a prolapse of the mucous membrane of the ureter and bladder results. That the portion of the bladder wall which surrounds the ureter is not included in the prolapsed tissue is proved, Boström thinks, by the absence of muscular tissue from the wall of the sac.

Burckhard, in his paper, modifies somewhat Boström's theory, holding that the primary cause of the abnormality lies not so much in the abnormal position of the ureter as in the congenital lack of musculature in the bladder wall. He also states that the dilated portion of the ureter does not originate, as Boström believes, in the portion just beneath the mucous membrane of the bladder, but on the contrary begins in the portion which lies within the bladder wall, the proof of this lying in the fact that in his case he was able to demonstrate unstriped muscle fiber in the wall of the sac. The absence of muscle fiber in the sac wall in Boström's case he explains on the grounds of disappearance from pressure atrophy.

Case 2.—*Anatomical Diagnosis.* Sloughing carcinoma of the uterus involving the vagina and bladder; involvement of both ureters in adhesions; hydro-nephrosis and hydro-ureter; kinking of the right ureter from the passage of the right ovarian vein over the dilated ureter; arterio-sclerosis; heart hypertrophy; recent vegetative endocarditis; emphysema of the lungs; diverticulæ of the intestine.

The following is the abstract from the autopsy protocol (Dr. Flexner) referring to the ureter:

The ureter on the right side is greatly dilated. The greatest dilatation is in the upper third, next the hilum of the kidney. At its entrance into the kidney there is a pyriform bulging of the ureter, the walls of which are so attenuated at this point as to permit of the slightly turbid but almost colorless contents being seen through them. The ureter just next to the hilum, and corresponding with the smaller part of the pyriform enlargement, has the size of a thumb. At a distance

of five centimeters from the hilum of the kidney a sharp bend occurs in the ureter, which is much constricted at this point by the passage over it of the ovarian vein, the walls of which are here thickened, but the lumen not entirely occluded. It is owing to the pressure from this vein that the upper part of the ureter is so much more dilated than the lower part, which will be described later. The pressure from above has caused the pushing downward of the upper portion of the dilated ureter, thus partly covering over the lower portion and causing an S-shaped bend or curve.

The lower portion of the ureter has a length of ten to twelve centimeters, and at the uterine end is embedded in firm adhesions. The dilatation of this part is somewhat less than that of the upper portion, and on an average it is about the size of the index finger. The lower part of the ureter contains the same faintly turbid fluid contained in the upper part. A probe cannot be passed from the slit up ureter into the bladder, even with the use of a moderate amount of force.

Remarks. In this case the hydro-ureter and hydro-nephrosis were evidently due in the first case to the inclusion of the lower end of the ureter in adhesions. The peculiar kinking, which was the interesting feature of the case, was due to the passage across the dilated ureter of what appeared to be the right ovarian vein, though instead of emptying into the inferior vena cava, as would normally be the case, it terminated in the right renal vein. As the vein was not in any way bound down, its mere tautness was evidently sufficient to cause compression of the dilated ureter.

We have been unable to find an account of a similar case.

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Discussion.

Dr. Kelly.—Prolapse of the ureter has been observed in women out through the bladder and even projecting from the external urethral orifice.

I had a case of colon bacillus infection about a year ago in which the urine taken directly from the kidney was examined a number of times. After washing out the kidney a great many times, and finding that I could not clear up the pus in the urine, as I had done in other cases, I concluded that there must be some mechanical cause to keep up the disturbance, and I cut down and removed a stone.

The condition on the right ride of this case is a very important one. Cases of hydro-nephrosis of lesser degree, 10–15 cc. or more, have been attracting my attention more and more. In all of them we find a diminished amount of urea in the urine, for the kidney has been somewhat impaired in its functions. It is important to be able to recognize the condition; it cannot be palpated through the abdominal walls, but can be made out by introducing my renal catheters in women. These cases must be handled carefully because of the increased liability of infection. If one side is hydro-nephrotic and the other side has suppurated, then we must proceed with unusual caution in any surgical interference. In a recent case the urinary analysis showed a percentage of urea on the sound side of 2.6 per cent. and only 0.3 per cent. on the hydro-nephrotic side.

Dr. Flexner.—We have had very scant opportunity in the pathological laboratory to make bacteriological examinations of cases of wound diphtheria, the case reported by Dr. Blumer being the second one in several years. The previous case, upon which I performed the autopsy, was associated also with the genito-urinary apparatus and followed the operation of perineal section for stricture of the urethra. Previously there had been cystitis, pyo-ureter and pyo-nephrosis. The diphtheritic process extended from the external wound through the bladder and ureters into the pelves of the kidneys, which were more or less completely involved. The micro-organism which was separated from the local inflammations was the staphylococcus pyogenes aureus.

Of course these cases are examples of diphtheritis, and not of diphtheria, and in the great majority of cases of so-called "wound diphtheria" the pyogenic cocci, and not the bacillus diphtheriæ, are the causative agents. Examples of wound diphtheria caused by the diphtheria bacillus have been reported, these having usually occurred in persons suffering from faucal diphtheria. Brunner has, however, found the bacillus diphtheriæ in cases in which no history of faucal diphtheria could be obtained.

NOTICE.

All inquiries concerning the admission of free, part pay, or private patients to the Johns Hopkins Hospital should be addressed to Dr. Henry M. Hurd, the Superintendent, at the Hospital.

Letters of inquiry can be sent, which will receive prompt answer, or personal interviews may be held.

Under the directions of the founder of the Hospital the free beds are reserved for the sick poor of Baltimore and its suburbs and for accident cases from Baltimore and the State of Maryland. To other indigent patients a uniform rate of $5.00 per week has been established. The Superintendent has authority to modify these terms to meet the necessity of urgent cases.

The Hospital is designed for cases of acute disease. Cases of chronic disease are not admitted except temporarily. Private patients can be received irrespective of residence. The rates in the private wards are governed by the locality of rooms and range from $20.00 to $35.00 per week. The extras are laundry expenses, massage, the services of an exclusive nurse, the services of a throat, eye, ear and skin or nervous specialist, and surgical fees. Wherever room exists in the private wards and the condition of the patient does not forbid it, companions can be accommodated at the rate of $15.00 per week.

One week's board is payable when a patient is admitted.

TUMORS IN THE MOUSE.

BY L. E. LIVINGOOD, M. D., *Fellow in Pathology, Johns Hopkins University.*

The necessity of broadening our knowledge of pathology as well as deepening it, has forced itself very emphatically before workers in this subject in recent years.[9-11] Especially is the study of morbid conditions occurring in animals used commonly in experimentation, of interest and importance, lying as they do in closest relation with our studies of the human conditions.

It has thus occurred to Dr. Welch, to whom my heartiest thanks are due for his happy instigation, that a more minute study of a series of tumors found growing spontaneously in mice in captivity would prove an interesting problem.

The many attempts at inoculating and grafting tumors, for the most part carcinomata, into animals, especially the more or less successful attempts recently made by Moran,[1] Boinet,[2] Mayet[3] and others,[9-12] have interested me to study the possible homology and analogy of these tumors to those found in human beings, and the discoveries of possible parasites, to a search in the field of etiology.

Tumors in certain domestic animals were noted and more or less carefully described by the ancients. Huzard in the XVIII century was the first to call attention to their frequency in carnivora. After 1825 we find various tumors in animals described by Trousseau, Leblanc,[4] Semmer[5] and others. Cadiot[6] (1894), in reviewing the carcinomata in dogs and horses, asserts that all animals will probably be found susceptible to carcinomata, which he claims to be the most frequent form.

Moran describes a tumor appearing spontaneously in a mouse, lying in the subcutaneous tissue but not attached to the skin. He describes it superficially as of tubular-gland type.

No. 1, of the series which I ask leave to bring before you to-night and of which Fig. 1 is a partial picture, was found in the right lung of a white mouse dying of experimental bacterial infection. It projected from the upper surface of the middle lobe as a small white boss about 5 mm. in diameter, slightly friable and apparently softer in the center. The lung tissue about it was congested. No other growths were noted.

Microscopically the boss presents the appearance of an adeno-carcinoma. At one point it may be seen arising from within a bronchus, growing as a papilloma within and, at one point, breaking through its walls and dispersing in the surrounding tissue. The greater part of the tumor is made up of infiltrating fingers of epithelial cells. The cells are of irregular columnar or polygonal type with oval vesicular nuclei. They are often arranged in single rows lining a long cul-de-sac, or they project into the surrounding tissue in solid masses. There is nowhere distinct basement membrane nor transverse section of a duct or tubule. The connective tissue stroma is very scanty, the infiltrating fingers alone seeming to restrain one another and causing, by mutual pressure, irregular growth. About the periphery and less markedly in the midst of the tumor there are areas in which the tumor has undergone disintegration, shown by fragmentation of nuclei and breaking down of cells.

The alveolar cells and connective tissue cells about the tumor have proliferated, giving the lung a carnified appearance.

No. 2 was removed during life under surgical precautions, from the neck and shoulders of a white mouse.

An alcoholic specimen of the tumor shows a small firm lobulated mass, partly encapsulated, about the size of a chestnut; the surface is irregular; the interspaces are filled with coagula. On section, however, the tumor presents a rather uniform white color and firm consistence. To this tumor is attached a small one of less uniform structure and color.

Macroscopically the appearance is that of sarcoma, but microscopically it is that of a true gland. It is divided into lobules by thick bands of connective tissue extending in from the dense fibrous capsule. These connective tissue elements show signs of proliferation.

The tumor is tubo-racemose in type. The tubules and acini are lined usually with a single layer of cuboidal or columnar epithelium, resting on a basement membrane. Frequently the lumina of the tubules are filled with cells forming solid epithelial cords, in which the cells are compressed and distorted. Again the lumina are wide and free. No ducts are apparent. The cells are throughout of the same character, although immediately under the capsule in some places they are flattened and compressed, looking like deeply staining fibrous tissue cells.

At one point the tumor elements have worked their way between the fibers of the capsule, at which point the capsule is hæmorrhagic. The smaller lobe is a lymphatic gland which has not been invaded, although firmly adherent to the capsule of the tumor at the point of infiltration. Its blood-vessels are much congested.

On the opposite side of this gland is a small nodule of normal glandular structure.

Several months after removal of this tumor there was a recurrence at the seat of operation (Fig. 2), and associated with this, on the death of the mouse, was found a metastatic deposit in the lung. This tumor was of the same type as the original one, an adeno-carcinoma, presenting three distinct appearances as shown in Fig. 2: 1) normal gland structure, in which the acini are frequently filled with cells; 2) more truly carcinomatous growth, in which the gland type is lost through the proliferation of the cells, although the clumps of cells still remain hemmed in by the basement membrane; 3) a dilated condition of the alveoli, leading to thinning of the walls.

No. 3 is a tumor projecting from the inner side of foreleg of a white mouse; with this was a metastatic deposit in the lung.

The tumor in alcohol represents a rather uniform lobulated growth about the size of a hickory nut, consisting of two hemispheres, lying immediately beneath the skin, to which, however, it is not adherent. It is distinctly circumscribed. Through the skin its nodular surface may be felt. On section it presents a uniform, firm yellowish surface; magni-

fied it shows a dense fibrous capsule enclosing the elements of a true carcinoma, consisting of long solid epithelial cords and culs-de-sac and, likewise, elements of more glandular appearance, in which acini are sometimes lined with a single, sometimes with a double layer of cubical epithelium. The epithelial elements are in certain areas separated by considerable young connective tissue and have atrophied. Certain areas present marked necrosis of epithelial cells, the lumina of some tubes being filled with necrotic elements.

The connective tissue stroma, which is quite abundant, is in places extremely vascular, and in others its cells are widely separated, giving it a myxomatous appearance.

There are several lung metastases. Fig. 3 shows a small one arising apparently within a lymph space.

No. 4. A tumor occurring in the axilla of a grey mouse, is about the size of a hickory nut, hard, nodular, appearing immediately beneath the skin, to which in places it is firmly adherent. It is of firm consistence and yellow color (alcoholic specimen). On cross section it differs from the other tumors in being more irregular in color and consistency. There are several dark, softer areas on its surface.

Microscopically the tumor is made up in part of irregular gland structure with a single layer of cubical cells lining the alveoli, but for the most part is composed of cords of polyhedral epithelium. It may be seen projecting up into the corium of the skin, but at no point is it in communication with the epidermal tissue. Certain areas are necrotic. In some places what appear to have been gland acini are now dilated spaces lined by a single layer of flattened cuboidal cells and containing a granular material, remnant of disintegrated cells. The connective tissue stroma shows signs of proliferation. In this, as in all the preceding tumors, karyokinetic figures were found in abundance in the tumor cells.

The 5th tumor (Fig. 4) represents one of several nodules, small, measuring 4 mm. in diameter, of granular appearance, projecting from the skin on the fore- and hind-leg of a wild mouse. These tumors were excised and sections show them to be pure adenomata of the sebaceous glands. Some of the gland acini appear normal, being filled with their peculiar opaque, coarsely granular epithelial cells with small round nuclei. The acini are limited by a distinct membrane. The cells lying next to it are small and compressed; as one approaches the center of the acinus they become larger and show the appearance of their peculiar degeneration, the nuclei becoming obscure and the protoplasm swollen. Some of the acini are distinctly cystic, partly filled with fine granular material derived from the degenerating cells. The dilated ducts may readily be traced at times through the hair follicles to the periphery. The epithelium of the hair follicles does not seem to have proliferated. Among the gland cells no distinct karyokinetic figures are to be made out.

Beneath the tumor the subcutaneous tissue has normal appearance, limiting all growth further downwards. The small glands found in almost continuous succession throw light on the presence of the one in tumor No. 3.

The type of these tumors is, in general, with exception of the last, adeno-carcinoma, some showing an almost pure carcinomatous appearance. And in this connection it is interesting to note that the macroscopic appearance is almost invariably that of sarcoma; a nodular surface, well circumscribed by fibrous capsule, uniform firm structure, which might naturally, as Cadiot holds, have led the older writers to place sarcoma as the most common tumor in animals. From this series carcinoma should certainly have that place. The elements making up the tumor and method of their growth differ in no way from those of growths occurring in human beings. Two of them give metastases which preserve the original type of structure and cells. One gives further evidence of its malignant nature by recurrence three months after removal. The last occurred as multiple tumors. The rate of growth of none was noted, except the recurrence of tumor No. 2, which was very rapid.

The position and character of all of them are suggestive of their point of origin. Three occur primarily about the neck and breast of the animals. All of these are superficial, lying immediately beneath but still not involving the skin. Their elements are not those of epidermal epithelium, but are distinctly glandular, and suggest at once as their point of origin the mammary gland. The origin of the last is obvious.

The occurrence of the primary tumor in the lung is interesting when we consider the rarity of that occurrence in man.

The capsule we must look upon either as a thickening of the original gland capsule or a proliferation and condensation of the connective tissue about the growing mass.

I may say in closing that in none of them, with the ordinary methods of staining, have I discovered anything which resembled the "coccidia" found by Ruffer and Walker,[7] which they wish to associate with the etiology of the condition, nor the blastomyces of Busse[8] and Sanfelice.[9]

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THE MALARIAL FEVERS OF BALTIMORE.

An Analysis of 616 cases of Malarial Fever, with Special Reference to the Relations existing between different Types of Haematozoa and different Types of Fever.

By WILLIAM SIDNEY THAYER, M. D., AND JOHN HEWETSON, M. D., *Assistants in the Medical Clinic of The Johns Hopkins Hospital.*

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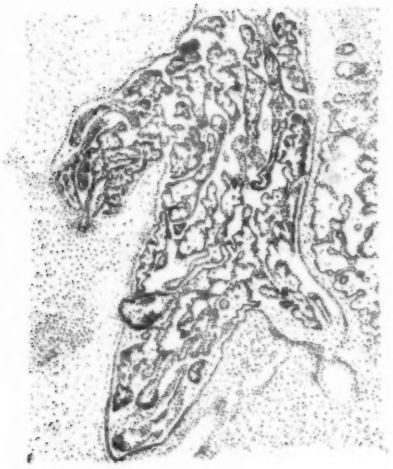


FIG. 1.
Adeno-carcinoma occurring primarily in lung of mouse.

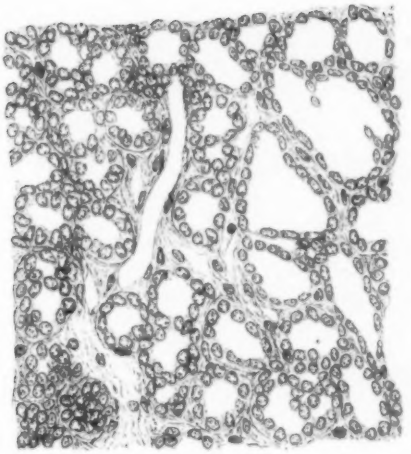


FIG. 2.
Recurrent Adeno-carcinoma in mouse. (In the breast.)

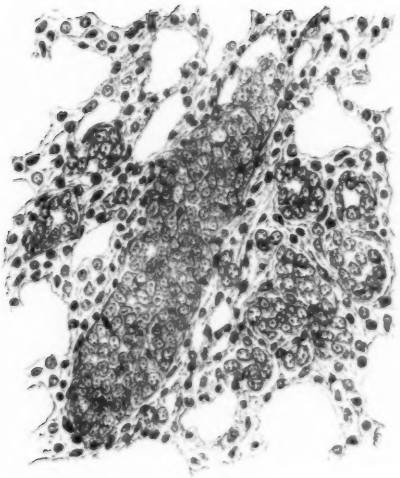


FIG. 3.
Metastatic Adeno-carcinoma in lung of mouse.

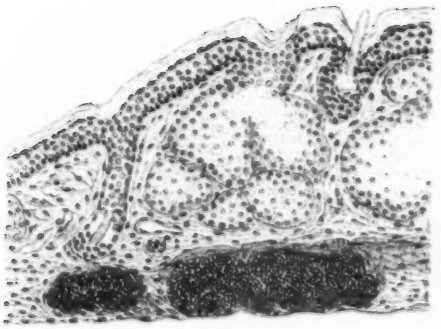
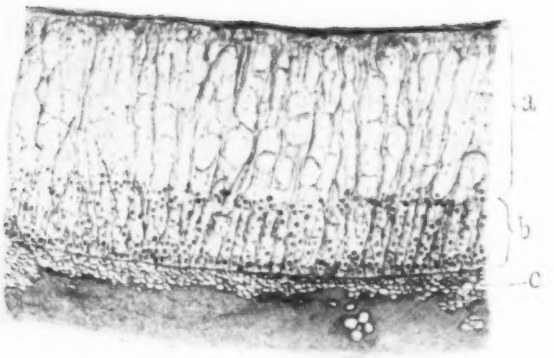


FIG. 4.
Sebaceous Adenoma on thigh of wild mouse.



CASE I.

a.—Atrophic degeneration of the retina in its anterior part. Disappearance of all the retinal layers as far back as the Internal Granular Layer. Müller's Fibres are wavy in their course and appear swollen.

b.—Remains of the Internal Granular, External Molecular, and External Granular Layers.

c.—Several layers of albuminous transudate.

CASE I.

Fibrillary Degeneration of the Vitreous Body.

The Friesenwald Co., Engravers and Printers.

THE ANATOMICAL CHANGES IN TWO CASES OF RETINAL DETACHMENT.*

BY ROBERT L. RANDOLPH, M. D.

I have selected the following cases as being fairly typical of the two principal conditions leading to detachment of the retina. Case I was a spontaneous detachment due to fibrillary degeneration of the vitreous, and Case II was where a small round cell sarcoma had pushed the retina away from the choroid.

Case I.—The detached retina as it sprung from the papilla looked like a funnel having a neck about one-fifth of an inch long, and which at this distance from the papilla commenced to assume the funnel-like shape. The retina was detached below all the way around to the ora serrata. Above and at a point one-sixteenth of an inch posterior to the ciliary muscle it was lying in position. From this point it turned backwards, and then passed directly down to a point which lay in the pole of the lens, and from here it took a course forward and then upward, and finally lost itself in the ora serrata. That part of the funnel which had an upward direction was thrown into numerous and intricate folds and enclosed in its meshes a mass of vitreous body, while that part which passed below was composed of the entire thickness of the retina, which appeared quite normal. The peculiarity of this portion was the absence of folds. The inner surface of the retina at the widest part of the funnel was covered with a thick mass of vitreous body, and the angle which was formed by the ciliary body in front and by the retina behind as it fell backwards and downwards from the ora serrata, was filled with coagulated material and fine fibrillæ, which latter passed forward and served to form numerous bridges across it. The ciliary processes were covered posteriorly with several layers of the vitreous fibrillæ. The zonula was not distinguishable as such, it no doubt being merged into the fibrillæ. That portion of the vitreous space lying between the retina and choroid was empty. No doubt we had a fluid here during life. At some points anteriorly could be seen what are described by Nordenson as the choroidal tufts, "chorioidalzotten," which appeared like little bridges uniting the retina and choroid. There was nothing worthy of note about the choroid, and the same could be said of the ciliary body, iris and lens. There was a good deal of material in the anterior chamber which was probably the transudate coagulated by the hardening process.

Microscopic changes.—The changes in the retina were very noticeable, and particularly in the anterior part of the eye. The anterior portion of the detached retina was the seat of the most marked degenerative changes, the retina itself resembling closely a reticulated tissue in which there was hardly a trace of the several layers. Posteriorly it was easy to recognize the various layers, but they gradually disappeared towards the ora serrata, and the only evidence of a layer was a single row of granules which marked the course of the external granular layer.

The layer of rods and cones was intact in several places, but this condition was generally found in the posterior half of the eye. At those points where the retina was thrown into very intricate folds this layer was more apt to be wanting, but even in this situation it was sometimes present. In those situations where the layer of rods and cones was absent, its place was filled with a mass of albuminous drops which were arranged in layers one on top of the other. On the inner surface of the retina one could see the meshes of the vitreous fibrillæ, which appeared to be exercising traction on the surrounding retina. This layer of fibrillæ was tolerably rich in nuclei.

In one place the retina had curved around so as to form a loop; on one side of this loop all the layers of the retina were to be seen, with the exception of the ganglion cell layer. The layer of rods and cones could be plainly seen as well as the external limiting membrane. On the opposite side of this loop the only layers which were present were the external granular layer and the external molecular layer, the latter to a very limited extent. The inner layers in this situation had been pulled out of all shape by the vitreous fibrillæ. The external granular layer presented generally a very irregular border line, appearing at points as papillæ-like projections due, I think, to the folding of the retina. The nerve fibre layer was not easily recognizable, and the layer which occupied its normal position, and which to a large extent was the nerve fibre layer, was the seat of numerous nuclei. The radiating fibres of Müller showed generally a wavy course. The line of demarcation between the nerve fibre layer and the ganglion cell layer was difficult to make out. This was no doubt to be attributed to the traction exerted upon the nerve fibre layer by the fibrillæ, and also to the very irregular course followed by the radiating fibres. As a rule the ganglion cells had dropped out of the section, and it was impossible to identify this layer.

An examination of the neck of the detachment, or, as I have called it, the neck of the funnel, showed no remains of the vitreous body. This neck appeared to be a mass of connective tissue, in which it was impossible to distinguish any of the layers of the retina, though it seemed to be made up largely of the granular layers. At the papilla there was no semblance of the retinal structure. There was, too, at this latter point a notable absence of blood-vessels. Upon the neck of the detachment, on all sides, several layers of albuminous drops rested. The fibrillæ were for the most part devoid of nuclei. They often looked as though they came directly out of the retina and made their way into the vitreous body, or as though they were prolongations of the radiating fibres, so intimate was their connection.

Choroid.—On the inner surface there were several layers of albuminous transudate resting on the pigmentary layer of the retina, which had remained behind, as it usually does in such cases. Increased nucleation was everywhere present throughout the choroid, and further than the points just mentioned there was nothing noteworthy in this part of the eye.

*Read in the Section of Ophthalmology at the Atlanta Meeting of the American Medical Association, May, 1896.

The vitreous body was wanting entirely in the posterior portion of the eye. Just behind the lens it seemed to be transformed into a granular debris devoid of fibrillæ, while in other portions it was composed apparently of nothing but the fibrillæ which have been described. The lens, iris and ciliary muscle were normal.

The chief points, then, about the pathological anatomy of this case were: 1. The widespread atrophic degeneration of the retinal layers, and especially of the layer of rods and cones. As a general thing the granular layers were the only layers that were preserved. 2. Swelling of Müller's fibres. 3. The presence of albuminous drops in various localities, and especially between the choroid and retina, and along the neck of the detachment; and finally the transformation of the vitreous body into fibrillæ. I may say in connection with this case that I am indebted to Dr. Mary E. Hennessy, of New York, for the specimen, who unfortunately was unable to furnish me with the history.

Case II.—The second case was that of a boy, aged seven years, who came to the Johns Hopkins Hospital early this spring. His parents had taken him to an oculist several months before; at that time his eye was not thought to be in a serious condition. He had been complaining for the last three weeks of severe pain in his right eye, and his parents had noticed a whitish yellow reflex from this eye. This reflex was very noticeable when he came to the hospital. The tension of the eye was decidedly elevated and the conjunctiva injected. Vision was completely gone. I advised enucleation and the eye was removed the following day. The macroscopic condition was as follows: The tumor involved almost the entire nasal half of the retina, filling up that side of the vitreous space both above and below. It extended back and seemed to proceed from the nasal side of the optic nerve, and advancing into the vitreous, stopped at a point about a quarter of an inch posterior to the lens. Over the area occupied by the tumor there was no trace of the retina to be seen. On its free side the growth was quite nodular, and one of the nodules projected across to the temporal side of the eye and almost reached the retina on that side. The retina in the temporal half of the eye was completely detached.

Microscopic changes.—The tumor was scant in intercellular substance and was made up of small round cells. Blood-vessels were tolerably numerous and they were usually filled with red blood corpuscles. Large areas of the growth failed to take on the hematoxylin stain, but stained with eosin. These were evidently necrotic areas. Hemorrhages were not infrequently seen. Wherever the tumor was present the retina was indistinguishable, the tumor having grown into it. The tumor cells were found in the optic nerve as far back as a quarter of an inch from the papilla. The vitreous body had been crowded over to the temporal side of the eye and had been transformed into the characteristic fibrillæ, which were evidently exerting traction upon the retinal folds. These fibrillæ had pulled the retina into intricate folds in the anterior portion of the eye, and just behind the lens the traction was enough to pull the retina backwards far enough to leave only a short narrow bridge separating the latter from the growth. The layer of rods and cones was nowhere visible, and just as in the first case, the ganglion cells in the ganglion cell layer had dropped out of the section. The internal and external granular layers were clearly definable, say from the equator around to the ora serrata. The retina posterior to the equator was very much thickened and broken down, failing to stain. At one point only, and for a very short distance, the external limiting membrane could be seen. The fibres of Müller were somewhat swollen and had a very wavy course, a course which more or less disturbed the position of the retinal layers.

The choroid nearly everywhere had been attacked by the growth, that is to say, large and small heaps of the sarcoma cells were present in this coat, and generally they were resting under the pigmentary layer, this condition extending around as far as the ciliary region on the nasal side, and on the temporal side a short distance from the papilla. There were no albuminous drops.

The principal changes in this case were the conversion of the vitreous body into fibrillæ and the atrophic degeneration of the anterior portion of the retina.

It would seem, then, that fibrillary degeneration of the vitreous body is to be found in both classes of cases. In the case of spontaneous detachment it was evident that the fibrillæ were largely concerned in pulling the retina away from its normal position, and from the arrangement of the retinal folds shrinkage or contraction from within must have been going on. In this case, as will be seen from the drawing, there was a considerable exudate consisting of layers of albuminous drops resting on the membrana limitans externa, which exudate no doubt played a part in separating the retina and choroid. These two conditions would explain the detachment in the first case and similar ones. In the second case the presence of the sarcoma was sufficient to lift the retina from its position, though even here it was evident at a glance that the retina was subject to a force from within which helped to pull it still further away from the choroid. I failed to discover a rent in the retina in either case.

In conclusion I may say that the most striking anatomical change in these two cases was the fibrillary degeneration of the vitreous body, a condition which, I think, is found to a more or less extent in every case of retinal detachment, and which no doubt is the chief element in the pathogenesis of the disease.

THE JOHNS HOPKINS HOSPITAL BULLETIN,

Volume VII.

The BULLETIN of the Johns Hopkins Hospital entered upon its seventh volume, January 1, 1896. It contains original communications relating to medical, surgical and gynecological topics, reports of dispensary practice, reports from the pathological, anatomical, physiologico-chemical, pharmacological and clinical laboratories, abstracts of papers read before, and of discussions in the various societies connected with the Hospital, reports of lectures and other matters of general interest in the work of the Johns Hopkins Hospital and the Johns Hopkins Medical School.

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THE BUBONIC PLAGUE.

[The substance of a report made to the Journal Club of the Johns Hopkins Hospital by SIMON FLEXNER, M. D.]

In October of 1894 an abstract of a report to the Journal Club of the Hospital, upon the subject of the bacillus of the plague, appeared in the Hospital Bulletin. The account there given of the micro-organism which had but a short time before been isolated from a number of cases of the black plague by Drs. Yersin and Katisato, and which was believed to be the cause of this devastating pest, was drawn from the reports of these investigators published at that time. The expedition sent by the Japanese government, at the head of which was Dr. Katisato, contained Dr. Aoyoma, whose mission it was to study the clinical and pathological features of the disease. Dr. Aoyoma became himself infected with the disease a short time after the beginning of his studies at Hong-kong, and although he recovered, the report of his studies has only recently appeared.* As was to be expected, these relate more particularly to the symptomatology and the pathological anatomy of the disease, although account is taken of the epidemiology and to a less extent of the bacteriology and of the mode of infection. In order that the first report given in the Bulletin may be in a manner complete, it is considered desirable to append an abstract of Dr. Aoyoma's recent report.

In May of 1894 the Japanese consul in Hong-kong announced to the Japanese government that the plague had appeared in Canton. Immediately following, a quarantine first of nine days and later of seven was set upon incoming ships, and Dr. Katisato, with his assistant Ishigami, and Dr. Aoyoma with his assistant Miyamoto and medical student Kinoshita, were sent to Hong-kong, where they arrived on the 12th of June. Through the kindness of Dr. Lowson they were permitted to arrange for their work in one of the rooms of the Kennedy Town Hospital, where on the 14th they had established themselves ready for work. Unfortunately Aoyoma and Ishigami became ill with the pest on the 28th of June, owing to which the studies which are here to be given were limited to fifteen days of active service. In this time 19 autopsies were held and 45 clinical cases studied, the latter more or less completely. In addition to these the opportunity of seeing a large number of cases in the Chinese hospitals had been embraced.

Respecting the situation of Hong-kong and the condition of the soil, its inhabitants and houses, the following may be stated: Hong-kong is one of the widest of the islands situated in the Gulf of Canton stream, and lies 142 km. southeast of the city of Canton, and 62 km. east of Macao, and is separated by a small body of water, which is used as a harbor, from the mainland. The island is mountainous, from two to five miles in length, and consists of granitic rock. Respecting the climate it may be stated that it is tropical, and the warmest months of the year are from March to November. The winter is also warm, and snow is not known in that locality.

Victoria, which is the principal town, extends from east to west along the north coast, between the sea and the mountainous background, and follows the latter, as it is built in part upon the mountain side. In the most easterly part we meet the barracks, villas, factories and the European shops. The westerly and middle parts, which are lower, are the Chinese quarters. The portion of the town which was most affected is known as Taiping-chan, which lies in the middle of the city. As regards the streets themselves, excepting that they are narrow, they are the equals of the best European streets. The houses, which are usually two stories in height and built after the European fashion, number about 7900, of which 6600 belong to the Chinese population.

The number of inhabitants of Hong-kong is difficult to ascertain and probably reaches the neighborhood of 250,000. The report obtained from the water-supply bureau gave 163,949, of whom 151,974 were Chinese. The overcrowding of the houses of the Chinese workmen has greatly increased during the past ten years. It is stated that in the ten years from 1881 to 1891 the number of inhabitants of the city increased 41 per cent., while the houses increased only $13\frac{9}{10}$ per cent. The densest population is found in Taiping-chan, where it would appear that in a house area of 0.173 acre 3740 Chinese live. The streets of this part are very narrow, the houses are two-storied, the windows small and few in number. The houses, which are long in form, are separated by partitions into two parts, each of which is further subdivided into a number of large rooms. In the earlier times one of these rooms housed a single family, but at the present, owing to overcrowding, these rooms have been divided by subpartitions into an upper and a lower compartment, and these compartments further by upright partitions, so that several rooms have been constructed out of the original ones, in each of which a family now lives. The average size of the main room is 26x14 feet by 10 feet high, and contains eight partitions averaging 7x6 feet by 7 feet high, over which a sort of loft is often built to increase the accommodation, and in a room of this description from 16 to 25 people live.

The canalization is constructed so that one system of pipes receives the washings from the rains and the other the sewage from the kitchens, etc. The first works perfectly, whereas the other is for the most part in a very bad condition, so that stagnations frequently occur and the sewage is dammed back upon the houses.

The city itself is provided with an excellent water supply, which in certain times is even subjected to filtration. The clothing of the Chinese is hygienically to be recommended. The only difficulty to be pointed out is, that although well conceived for the purpose, it is never under any circumstances subjected to washing, which fact is equally true of their bedding. The personal habits of both the men and the women are almost beyond belief in their crudeness and neglect. Cleanliness on their part, or anything approaching it, is an absolutely unknown art.

* Mittheilungen aus den Medicinischen Facultät der Kaiserlich-Japanischen Universität, Band III, No. II, Tokio, 1895.

As regards the cause of the plague, it may be said that Katisato discovered bacilli in the blood and in the lymphatic glands which differed somewhat in their morphological characters but which agreed in their cultural properties. According to Katisato, the bacillus which appears in the blood resembles the organism of chicken cholera, possesses a capsule, the middle portion staining very faintly; while the bacillus obtained from the lymphatic glands is somewhat longer, has rounded ends, and stains more uniformly than the other. The bacillus obtained by Yersin is stated to have rounded ends, to be easily stained with the aniline dyes, and to be decolorized with Gram's method. The ends again stain more uniformly than the middle part. According to Katisato, the organism would at times stain by Gram's method, and at others not. Aoyoma, however, observed that those contained within the lymph glands were decolorized, and those in the blood stained by this method. The number of organisms contained within the blood is usually not large, and may be so small that it is necessary to prepare a large number of cover-slip preparations in order to find sufficient for a diagnosis. On the other hand, they are found abundantly in the affected lymphatic glands.

The study of the tissues has shown that in the lymph glands a variety of bacteria may be met with. As a constant and predominating species the lymph gland bacillus of Katisato is found, although in rare cases micrococci predominate. Careful observation, however, shows within these masses greater or less numbers of the pest bacilli, the streptococci occupying the blood-vessels rather than the gland substance. The pest bacilli in the tissues stained less intensely in alkaline methylene blue solution than the streptococci, and the staphylococci least of all. It is stated that while the streptococci retain the Gram stain, the bacilli and the staphylococci do not. It is suggested by Aoyoma that the forms described by Katisato as occurring in the blood and retaining the Gram stain may have been pairs of cocci and not bacilli at all. He regards the association of the bacilli and cocci as of great importance, inasmuch as in the greater number of instances the affected glands suppurate, while a very small fraction do not. Hence it is considered that the suppuration is caused not by the plague bacilli which are always present, but through the action of pus-producing bacteria which entered along with the former or later than these; and Aoyoma has further found that in suppurating glands the plague bacilli are either much diminished in numbers or have entirely disappeared.

It may be recalled that in the first reports of Katisato and of Yersin they stated that the bacilli might enter the body first through the respiratory tract, second the digestive tract and third, excoriations of the surface. Aoyoma, on the other hand, expresses the opinion that in the great majority of cases, if not in all, the entrance is through external wounds. He points out that physicians and nurses who are in attendance upon infected individuals and spend much time in the places in which the sick are kept, rarely become infected with the disease. In this epidemic, of all such persons who were in attendance upon the sick, only three Japanese physicians and one Chinese physician became infected, the nurses having entirely escaped. During the prevalence of the epidemic 300 English soldiers volunteered to cleanse and disinfect the Chinese pest-houses. Of these only ten became affected with the disease. Thus it would appear as though an actual pest atmosphere did not exist and that the infection did not take place through the inspired air. Moreover, Aoyoma did not observe that the tracheal or bronchial glands were in a condition of intense inflammation, which he presumes would have been the case had the bacilli invaded through the air passages.

Respecting the question whether the organisms are taken into the body through the drinking water or with the food, it may be said that the Chinese do not drink unboiled water, and never under any circumstances eat uncooked foods. That portion of the town (Taiping-chan) which was most infected, and in which the hygienic conditions were the worst, received its drinking water from the general supply. It is true that Katisato was able to cause infection in mice by introducing the bacilli into their stomachs through glass tubes, but it is stated by Aoyoma that Katisato does not any longer regard these experiments as being certain proof of infection through the alimentary tract. It is noteworthy that at autopsy the lymphatic apparatus of the stomach and intestines and the mesenteric lymph glands were never found greatly inflamed, and the last contained very small numbers of the bacilli only, or in certain cases none at all. Hence it is stated that all physicians who observed this outbreak of the pest were forced to the idea that the bacilli entered chiefly through external wounds.

In the great majority of cases the deep inguinal and the axillary glands, and in a small number of cases the superficial inguinal glands, of one side were first affected and afterwards other glands became involved. This fact is explicable only upon the assumption that the organism entered through small defects of the skin which were present either on the feet or the hands; and as the working class of Chinese usually go barefoot, such small defects can easily be imagined to exist. Further, as is known, the lymphatic vessels of the feet run to the deeper and lower inguinal glands, thus exposing these first in the great majority of cases. The superficial inguinal glands receive the lymphatics of the penis and the skin over the lower portion of the abdomen, and these are but seldom primarily affected. Of the nine Japanese whom Aoyoma observed, two women showed affection of the axillary glands, one of the submaxillary glands, whereas in the other no glandular affection could be detected, notwithstanding the fact that the bacilli were found in the blood. Of the Japanese men, four showed swelling of the axillary glands, and one only of the inguinal glands. This is interesting when it is considered that the Japanese do not go barefoot. It may also be mentioned that among the Chinese the women show affection of the axillary rather than of the inguinal glands.

The wounds through which the infectious agent enters show, as a rule, no reaction. Notable exceptions to this statement are his own case, in which a lymphangitis was present, and that of his assistant, Nakahara, who succumbed to the disease and in whom lymphangitis was also observed, in both cases beginning in the hand and extending towards the axilla. As regards the manner of diffusion of the bacilli, nothing new has been offered in this report. The period of incubation of the disease is given at from two to seven days; and as regards

the age and the sex of those affected, it may be said that the greater number of cases occur in young males.

The following table gives the relative proportion of men, women and children affected:

Men	62.40 per cent.
Women	19.23
Boys	8.92
Girls	9.45

It is worth noting that Aoyoma himself did not observe a single case in newly-born children or sucklings, although an English physician, Dr. Lowson, claims to have seen five or six cases among the latter.

The mortality in Hong-kong from the beginning of the disease until the 2nd of September is given as follows:

	Number Affected.	Number Died.
Europeans	11	2
Japanese	10	6
Manilanese	31	1
Urasinese	3	3
Indians	13	10
Portuguese	18	12
Malayanese	3	3
West Indians	1	1
Chinese	2619	2447

Symptomatology. The symptoms of the disease during the last plague were not, as was stated by most authors, protean, but they were quite simple. The disease began for the most part without prodromata, with a chill, or even in the first instances with pain and swelling of the glands and with succeeding chill and fever. Prodromata when present were usually short and varied in duration from a few hours to two or three days; or perhaps somewhat longer. The symptoms in the prodromal stage are prostration, headache, nausea, vomiting, loss of appetite, vertigo, and only rarely pains in the lumbar region or in the back. In the cases of the affection of the more intelligent population, even before the outbreak of the fever, slight swelling and pain were noted in the glands; whereas in the more obtuse Chinese these slighter phenomena were not noticed.

The temperature rises quickly to 39° or 40° C. or even higher, and remains high during the progress of the disease. Delirium sets in early, for the most part after the second day, and continues day and night, although in the lighter cases it may be absent during the day. On the other hand, severe cases occur in which from the beginning until death supervenes the functions of the brain are intact. The pulse is usually of good volume, as a rule is dicrotic and varies in frequency from 90 to 120 per minute. The spleen is palpable usually after the second or third day. It rarely can be felt more than a few cm. below the costal margins. The liver also is usually enlarged and palpable.

The urine is in most instances of dark color, cloudy, contains albumen, and does not, as a rule, give the diazo reaction. A few casts, either hyaline or granular, and white corpuscles are usually present. Very rarely the urine contains blood.

After the first or second day the glandular affection becomes more marked, and those glands first involved may reach the size of an egg. The pain increases with the growth in size, although in some cases it may be absent excepting upon pressure. The glandular affection is characteristic, inasmuch as it begins in one group and then involves in succession others, as for example first the inguinal, then the axillary, then those of the neck, and finally the submaxillary glands. The glands of the neck, of the elbow and the knee are seldom primarily affected. Only very rarely do several sets of glands become enlarged at once. Very soon after the swelling of the glands the periglandular tissues become involved and then later the skin. In the milder cases, suppuration may not occur and the swelling gradually diminish and finally disappear. On the other hand, suppuration may occur even in glands but little enlarged.

The temperature rises rapidly to 39 or 40 degrees, and in rare cases to 41½ degrees. In other instances the rise is more gradual. After remaining continuous for three or four days, there may be a critical fall, or the decrease may be gradual. In severe cases which recover the fever lasts from one to three weeks, and towards the end presents an irregular and remittent type. In not a few cases after the temperature has returned to the normal at the end of the first or the beginning of the second week there is a relapse, the fever now assuming a remittent character. The remittent fevers are suppurative; the fever is very rarely from the beginning remittent and irregular.

Actual hemorrhages into the skin were observed but once by Aoyoma, although congested areas are not infrequent. These latter areas disappear upon pressure and are believed to be caused by the bites of mosquitoes. Respecting the question of the appearance of an exanthematous eruption, it is stated that a rapidly disappearing erythema may occur. Symptoms referable to the brain, with the exception of the delirium, were very rarely observed. Fibrillary twitchings occurred before death, and actual convulsions were seen in very rare instances. In only one case was opisthotonus observed.

In the *Foudroyante* cases death may occur before any considerable glandular swelling can be made out; in the severest cases taking place on the second day. As a rule, death occurs from the second to the eighth day, and on an average on the fourth day. As suppuration of the glands rarely occurs before the tenth day it was not observed in these more rapid cases. When death takes place late in the course of the disease it may be due to a secondary pyæmic infection. The suppuration of the glands may continue for months, so that the convalescence of the patient is rendered very slow and tedious. When suppuration does not occur the glands gradually become smaller, although the enlargement may not entirely disappear for two or three months.

Complications are stated to be quite frequent. Of these, nephritis occurs quite commonly in the severer cases. It develops as early as the third or fourth day of the disease, is accompanied with the appearance of a moderate amount of albumen in the dark red urine, and microscopically hyaline and granular casts, as well as white and red blood corpuscles, are found. Œdema was rarely seen, and when present, of light

grade, and anuria was never observed. The blood which is present in the urine is not derived from parenchymatous hemorrhages, but from small extravasations into the mucous membrane of the pelvis of the kidney and the bladder. Abscess formation in addition to the lymph glands was observed in the liver, lungs and other organs in the later stages of the disease. Icterus of a light grade, and presumably of catarrhal origin, was often present; in one case it reached a very high degree, and at the autopsy it was found that the common duct had been pressed upon by a group of enlarged lymphatic glands. Serous pleuritis occurred but seldom, and seemed when present to be associated with the enlargement of the axillary glands. Pneumonia was seen in a single instance only, but bronchitis was much more common. Rarer complications are periostitis, lymphangitis, furunculosis of the skin, phlegmons which have their origin in the suppurating glands, carbuncle, singultus, and bloody stools.

Respecting the question as to whether cases of the pest without glandular affection ever exist, it may be said that in three cases which came to autopsy and which were proven to have died of the plague, enlargement of the glands was not made out during life.

The blood presented a dark red color, and the estimation of the corpuscles showed that the red corpuscles were only inconsiderably or not at all diminished, while the white were always increased. The number of white corpuscles per cubic mm. varied from 20,000 to 200,000; a control count of normal blood in a Chinese gave 10,000 white corpuscles to the cubic mm. The increase in white blood corpuscles is in the poly morpho-nuclear neutrophilic variety. Eosinophilic cells were very rarely seen. It is stated that the blood platelets were increased in number.

During the short time that Aoyoma carried on his studies he made autopsies upon 19 cadavers. The following is in brief the result of his studies of these cases: There is not infrequently a post-mortem rise of temperature; in one case the temperature taken four hours after death in the rectum, with a thermometer which registered 43 degrees, could not be estimated because the mercury was driven to the top of the capillary tube. Post-mortem muscular contractions also occurred in a similar manner to those observed in cholera. The affection of the lymph glands in various regions of the body has already been referred to, and it remains to say that in no case did he find evidence of a primary affection of the pleural or peritoneal lymphatic glands. No matter in which part of the body the glands are primarily affected, the entire lymphatic apparatus of the body shows at least some swelling, and perhaps congestion as well. With the exception of minute ecchymoses nothing abnormal was observed in the heart. The lungs and the pleura were not the seat of inflammatory changes, although in the latter, in certain of the cases of primary axillary affection, an increased amount of fluid existed in the pleural cavity. The spleen was enlarged, and sometimes considerably so. The kidneys showed the lesions of cloudy swelling, and often were congested. Small hemorrhages occurred in the mucous membrane of the pelvis. The liver was enlarged and hyperæmic and the seat of parenchymatous degeneration. The stomach and intestines showed more or less injection of the mucous membrane and increase of the mucous section. The pia arachnoid was as a rule hyperæmic and very œdematous. Purulent inflammations were never present in this situation. In few cases a moderate number of small hemorrhages were observed in these membranes. The fluid within the ventricles was moderately, never greatly increased. The substance of the brain showed a moderate œdema and numerous hemorrhagic points. In one instance an extravasation of blood the size of a bean was found in the medulla oblongata, and in another one of the same size occurred in the pons. The pia arachnoid of the spinal cord was hyperæmic and œdematous. Lesions were not found in the cord itself.

The increase in size of the lymphatic glands depends upon several factors, namely, hyperæmia, exudation, hemorrhage, hyperplasia of the gland cells, and great development of bacteria. The bacilli which are present are found in the earlier stages in the lymph spaces about the follicles, and later they are found within the follicles, the lymph sinuses and the medullary cords. The cells of the affected gland undergo various degenerative changes and may become necrotic. They lose their nuclei in the latter case, and a variable amount of nuclear detritus is present among the degenerated and necrotic cells. The hemorrhages are not limited to the gland itself, but may be found, as well as greater or less œdema, in the periglandular tissues. The usual fate of the enlarged glands is to suppurate, although in certain cases the swelling may disappear without suppuration and the glands return to normal; while in still others a fibroid induration may result. The suppuration is either of the nature of simple abscess formation, or preceding this there may be a necrosis of the gland substance; in certain cases the suppuration does not remain limited to the glands, but extends into the periglandular tissue. Sections of the lymph glands showed a variety of bacteria. It is stated that in the primary localization various bacteria may be associated. Among these can be distinguished the pest bacilli and cocci, and among the latter both streptococcus and staphylococcus forms may be discovered. Aoyoma considers the association of these organisms as very important in determining the suppuration or non-suppuration of the affected glands. The spleen usually shows the presence of large numbers of bacilli, and among these more rarely micrococci. The pest bacilli were also, though not constantly, found in the interstitial substance of the kidneys and in the glomerular capillaries. They were also present in the inter- and intra-acinous tissues of the liver. The mesenteric glands sometimes contained the bacilli in small numbers; it is not stated whether or not they were found in the structures of the central nervous system.

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ABSOLUTE ALCOHOL AS A DISINFECTANT FOR INSTRUMENTS. A BACTERIOLOGICAL STUDY.*

BY ROBERT L. RANDOLPH, M. D.

For the past eight years I have employed absolute alcohol as a disinfectant for all cutting instruments used in operations upon the eye, and recently I instituted a series of bacteriological experiments to test the value of this agent as a practical disinfectant. The cataract operation demands a keener knife, probably, than any operation in surgery, and the peculiar objections to heat for sterilizing cutting instruments led me to adopt the use of absolute alcohol as the best substitute for heat. I have satisfied myself again and again that not only does moist heat, but even dry heat dulls the edge of instruments, and this I understand has been the experience of many surgeons. In making this contribution to our knowledge of alcohol, it is not with the idea that I am introducing a new disinfectant, for I am well aware that there are not a few ophthalmologists who use it as an agent for sterilizing instruments. No matter though how well satisfied we may be with aseptic measures, we cannot understand why they are satisfactory, or, in other words, how much they contribute to our success, until these measures have been subjected to bacteriological tests, and, as far as I know, no exhaustive series of tests of absolute alcohol as a disinfectant for instruments has been made.

The experiments of Koch go to show that alcohol possesses inferior germicidal qualities, in so far as its action upon the spores of the anthrax bacillus is concerned, the spores retaining their vitality after a submersion of one hundred and ten days in alcohol. This power of resisting the action of germicides exists in a marked degree in the case of the spore-producing organisms, as is shown among others by the works of Globig† and of Reinicke.‡ It is evident that in the case of the spores of the anthrax bacillus at least, absolute alcohol is practically useless as a germicide, but the negative results of Koch should not be taken as an evidence that absolute alcohol has no value whatever as a disinfectant. This is true only in so far as one organism is concerned, and that, too, an organism which, as far as we know, surpasses nearly all other bacteria in its vitality. It does not seem practical, then, to take Koch's results as a criterion for the germicidal value of absolute alcohol.

My experiments were undertaken at first to control, as it were, and to throw some light, from a bacteriological point of view, upon the method which I employ for sterilizing instruments in operations on the eye. These experiments were not intended to demonstrate the effect of alcohol upon any special organism, but to ascertain the value of this agent as a disinfectant for every-day conditions in eye surgery. The question arises, why not determine the effect of absolute alcohol upon some one or more of the commonly met with pathogenic organisms, for instance the so-called pus organisms, and be guided in my conclusions by results reached in this manner? We know for certain that the pyogenic bacteria are concerned in the production of many serious affections of the eye and its appendages, and that in those cases of sloughing cornea following the operation for cataract, to say nothing of panophthalmitis, one or more varieties of pyogenic cocci have been often found present in the affected tissues. No doubt many a staphylococcus and streptococcus infection has been conveyed to the eye by the instruments. There are practical reasons, though, for not approaching the subject from this point of view. The line between pathogenic and non-pathogenic organisms is not sharply drawn. Organisms which ten years ago were regarded as harmless, have been since shown to possess, under certain conditions, distinct and intense pathogenic properties. Take for instance the bacillus coli communis, the bacillus prodigiosus and the aspergillus fumigatus. Any one of these bacteria I have found, when introduced into the eye, will call forth the most intense inflammation. The investigations of de Schweinitz, Haab, Poplawska, and of myself, go to show that other than the so-called pyogenic cocci are met with which are capable of producing the most intense panophthalmitis. However valuable observations conducted on these lines might be, they would not tell us whether alcohol protects us from a host of other bacteria which under certain circumstances are just as pathogenic as the staphylococci or streptococci. These were my main reasons for not selecting a special organism to test the efficacy of absolute alcohol as a germicide.

Fürbringer* first called attention to the value of alcohol as a disinfectant for the hands. His work has been gone over by Reinicke (loc. cit.), who has added a long series of most exhaustive experiments bearing upon this question of hand disinfection, and he agrees with Fürbringer in attributing valuable qualities to alcohol as a disinfectant for the hands. Reinicke employed in his experiments permanganate of potash and oxalic acid, sublimate soap, carbolic acid, lysol and trikresol, and compared the results obtained with these agents with the results obtained by disinfecting the hands with alcohol, and his conclusions were as follows: After first washing the hands for five minutes in hot water, using soap and a nail brush, then following this by scrubbing them from 3 to 5 minutes with 90 per cent. alcohol, he found them almost always absolutely free of germs. He says finally that the quickest disinfection that can be relied upon is scrubbing the hands for five minutes in alcohol. His results were confirmed in the main by Krönig,† Ahlfeld‡ and Schaefer,§ though these

* Read before the thirty-second annual meeting of the American Ophthalmological Society, New London, Conn., July, 1896.

† Ueber einen Kartoffelbacillus mit ungewöhnlich widerstandsfähigen Sporen. Zeitschr. f. Hygiene, Bd. III, 1888, S. 322.

‡ Bacteriologische Untersuchungen über die Desinfection der Hände. Archiv für Gynaekologie, Bd. 49, S. 515–553.

* Untersuchungen und Vorschriften über die Desinfection der Hände des Aerztes nebst Bemerkungen über den bakteriolog. Charakter des Nagelschmutzes. Wiesbaden, 1888.

† Centralblatt für Gynäkologie, 1894.

‡ Monatsschrift für Geburtshülfe und Gynäkologie, 1895, Heft 3.

§ Therapeutische Monatshefte, Juli 1895.

observers differed in some points as to the exact action of alcohol.

Reinicke thinks that the alcohol in taking up the fat takes up the bacteria which are on the hands, and thus the bacteria can readily be washed away (*abgespült*).

Krönig is of the opinion that alcohol, from its dehydrating and astringent power, changes the skin so that the bacteria are held fast in the shriveled epidermis, and in this manner that they are rendered inactive.

Ahlfeld, however, believes in the germicidal power of alcohol and submits this test: Thirteen people were made to wash one of their hands for three minutes in hot water, using soap and a brush, at the same time the finger-nails were trimmed and cleaned. The hands were then rinsed in sterile water. Ahlfeld then removed some of the dirt beneath the finger-nails with a small splinter of wood, and dropped the latter into bouillon. Another finger-nail was treated in the same manner, and the piece of wood was dropped into a small glass containing ½ ccm. of alcohol. The piece of wood was always small enough to be completely covered by the alcohol. The same individuals were then required to repeat the cleansing process with the other hand, but instead of using soap and water, the hand was scrubbed for one minute in alcohol, and inoculations were made from the finger-nails in the same manner as in the first series. The results were as follows: In those cases where the cultures were made from finger-nails which had been washed in soap and water, colonies were present in every instance but two; while in those cases where the alcohol was employed as the cleansing agent, the tubes remained sterile. In the twelve cases where the infected particle of wood was allowed to remain in the ½ ccm. of alcohol for two days after evaporating the alcohol and filling the vessels with bouillon, the latter were found to be sterile after a certain length of time. These tests certainly indicate that alcohol possesses germicidal power.

Schill and Fischer* found that when tuberculous sputum was mixed with alcohol in the proportion of five parts of the latter to one of the former, the bacilli were rendered inactive, as was shown by inoculation experiments. Yersin† found that pure cultures of the tubercle bacilli were destroyed by five minutes exposure to the action of absolute alcohol.

I might add that Green of Birmingham, England, has recently repeated the experiments of Reinicke and failed to confirm them, but his experiments are very few in number and his work is not yet completed. His communication appeared in the Deutsche med. Wochenschrift for June 4th.

As I remarked before, I have been unable to find any experiments bearing upon the efficacy of alcohol as a disinfectant for instruments.

The scheme followed by me in these experiments was as follows: A porcelain-lined tray ten inches long, two inches deep and five inches wide was first sterilized by dry heat. The instruments were then taken from the case and laid in the tray. Squibb's absolute (98–99⅔ per cent.) alcohol was poured on the instruments till they were completely covered, and then the tray was covered with a sterilized top. The instruments were allowed to remain in from a period ranging from fifteen to forty minutes. Only once, though, did they remain in the extreme limit; this was in the first series, where a great many instruments were sterilized at one time, and necessarily the last instruments taken from the alcohol had been immersed for a much longer period, namely, forty minutes. Agar tubes were used for the inoculating medium. Each instrument was taken from the alcohol with a pair of long forceps (which had been sterilized by holding them in a flame), and after being plunged once in sterilized water it was then pushed down into the agar. I may say here that each tube was stabbed at least three times, and the majority of tubes were stabbed five or six times, so that every portion of the instrument which would be likely to come in contact with the eye in an operation was rubbed against the culture medium. The instrument remained in contact with the agar from 20–30 seconds, which is longer than the knife remains in contact with the eye in the operation for cataract. The tubes were then placed in the thermostat at the temperature of the human body and allowed to remain for at least three days.

Fresh alcohol was of course used at every sterilization of the instruments. I have divided these experiments into three series. The first series consisted in the inoculation of one hundred tubes with eye instruments which had been sterilized in the way described. The following instruments were sterilized:

Graefe's cataract knives	7
Fixation forceps	6
Iris forceps	4
Iris knives	4
Lereich's forceps	1
Desmarre's pincette	1
Canaliculus knives	5
Scalpels and bistouries used in lid operations	12
Strabismus hooks	6
Lid retractors	4
Foreign body needles	4
Iridotomy scissors	2
Discission needles	4
Cystotomes	4
Scoops	2
Hooks for tearing capsule	3
Beer's cataract knives	6

And to these seventy-five instruments were added twenty-five nails. These nails were three and one-half inches long and one-eighth of an inch thick. It may be said that the nails had been lying for nearly a year in an open box about twenty feet from where all the autopsies of the Johns Hopkins Hospital are made, and it is almost certain that they were in consequence infected, and doubtless many of them with pathogenic bacteria.

Out of one hundred tubes inoculated in this manner there were five infections. It matters little as to the nature of these infections, for, as I have said before, the probabilities are that almost any if not all bacteria when introduced into the eyeball will cause inflammation, so that I did not concern myself

* Mittheilungen aus dem K. Gesundheitsamte, Bd. II, 1884.

† Ann. de l'Institut Pasteur, t. II, 1888, p. 60.

as to the properties of the bacteria found in the five infected tubes further than that three of the growths looked as though they were air bacteria, from the fact that they were more or less colored, and cover-slips showed that they were very gross. One of the organisms somewhat resembled the staphylococcus albus, but I am of the opinion that it was too large.

I confess that I was surprised at the result, for I thought that I would get more air infections, and also that the bacteria present on the nails at least would withstand the action of the alcohol.

Another more crucial test was then made: Seventy-five other nails were taken from the same box, and, as in the first instance, they were sterilized by allowing them to remain from fifteen to thirty minutes in absolute alcohol. Instead, though, of simply stabbing the agar, the nails were pushed into the agar as far as they would go and allowed to remain there. The tubes were then placed in the thermostat for three days. Nine infections resulted, or, in other words, nine tubes had growths in them. Five of these growths were almost certainly the result of infections which occurred after the nails had left the alcohol; two of these five were mold.

It is proper to say that all these experiments were made in the Pathological Institute, and furthermore in two rooms adjoining the autopsy amphitheatre. The conditions, then, for obtaining sterile tubes, or rather the conditions for testing the disinfectant properties of alcohol, were not favorable. It is not improbable that had these experiments been made in a room freer from chances of accidental infection from the air, that I would almost surely have gotten a greater number of sterile tubes. As it was, the results were surprising, especially in the case of the nails, and for reasons stated above.

I have often heard the remark made that eye instruments, from the manner in which they are kept, are not so apt as are other instruments to be unclean. This is probably so, but it is no excuse for relaxing antiseptic precautions in eye operations. In order to ascertain how many instruments in a given number were clean, that is to say bacteriologically clean, I made the following test with fifty instruments taken at random from my own case of instruments and from the hospital case. Some of the instruments had been used the day before and others not for a week previously. After use the instruments are usually dipped in warm water and then wiped with a soft linen rag and returned to the case. Instruments which had been treated in this way were taken, as I have said, at random from the case and plunged several times into agar tubes. Fifty experiments were made in this series, and in sixteen cases the tubes remained sterile. It is certainly surprising that so many sterile tubes followed these inoculations, and while this series shows that the measures we adopt for cleaning our instruments immediately after an operation possess decided advantages, it also goes to show that the majority of instruments, even when treated with our usual care, are infected. I made no examination of the infected tubes.

Thinking that a fitting conclusion to this work would be to ascertain the effect of absolute alcohol upon the pyogenic bacteria, I made the following experiments, fifty in number. Fifty eye instruments were first sterilized by heat and then infected with a pure culture of the staphylococcus albus in the following manner: A platinum loop was passed into the tube containing the growth of the staphylococcus albus, and gently drawn across the latter and withdrawn, and rubbed over that part of the instrument which is brought into contact with the eye. The instruments were then placed in a tray (which had been sterilized by heat) and one-half a pint of absolute alcohol was poured over them. Twenty minutes were allowed to elapse and each instrument was taken out with sterilized forceps, and that part which had been infected was plunged several times into an agar tube. The results were as follows: Forty-three tubes contained pure cultures of the staphylococcus albus. As to the seven tubes: one was sterile, one was infected with a large micrococcus, one contained a mold, another the bacillus subtilis, and the other three tubes contained bacilli, which were characterized by their very large size and by the luxuriance of their growth, and probably were air bacteria.

These results, to say the least, would seem contradictory when compared with the results of the experiments recorded in the first part of this paper, experiments which pointed to the undoubted value of alcohol as a disinfecting agent. We must consider this fact, though, in this connection, that when we infect an instrument with an organism in pure culture the infection is exceptionally, and I might say unnaturally, virulent, or in other words, that no instrument which has been infected accidentally by exposure to the various conditions surrounding us in every-day life could be so septic as the instrument infected artificially or infected in the manner described in the last series of experiments. The organisms are present in far greater numbers and they exist in their purity. Such a condition is practically never met with. The chance infection which happens to everything which is exposed for any length of time to the air is of the mildest character, even when the organisms are pathogenic, as compared to the infection with an organism in pure culture.

It is not unlikely that in the first and second series of experiments some of the instruments were infected with pyogenic bacteria, but these bacteria were present in too small numbers and under conditions too unfavorable to withstand the action of alcohol.

It is evident that the alcohol in the first and second series was adequate for disinfecting purposes, but it is equally true that alcohol is totally inadequate for disinfecting instruments which have been infected with the staphylococcus albus in pure culture, and this might contraindicate our relying upon absolute alcohol for disinfecting instruments which had been used in an operation when the pyogenic organisms are present in great numbers—as for instance, in panophthalmitis.

CONCLUSIONS.

1st. That in a given number of eye instruments, by far the majority are infected by exposure to the air.

2nd. That absolute alcohol would seem a valuable disinfectant for instruments infected under the conditions which ordinarily surround us in every-day life. This conclusion seems warranted by the results obtained in the first and second series of experiments. Attention may be called to the fact, too, that in the second series the nails were all without

a doubt infected, and it might be said that they had been exposed to conditions which, to say the least, were extraordinarily favorable for infection, so that this series, I think, is strongly suggestive that alcohol possesses disinfectant properties of no little value.

3rd. That the septic character of instruments infected with a pure culture of staphylococcus albus is not altered by exposure for twenty minutes to the action of absolute alcohol.

I may add that the alcohol employed in these experiments was Squibb's absolute alcohol, which is supposed to have a strength varying from 98½ to 99$\frac{9}{10}$ per cent. This is the grade of alcohol which I use in operations.

PROCEEDINGS OF SOCIETIES.

THE JOHNS HOPKINS HOSPITAL MEDICAL SOCIETY.

Meeting of February 3, 1896.

Dr. FLEXNER in the chair.

Generalized Melanotic Sarcoma.—Dr. BLUMER.

Dr. BLOODGOOD.—As I remember the clinical history of the patient from whom the specimens came, it was as follows: An old lady, some 70 years of age, presented herself to the dispensary last August, with a pedunculated tumor in the right axilla. The tumor was perhaps 3 or 4 cm. in diameter and its pedicle perhaps 2 cm. long, but not larger in diameter than the finger. It seemed to be a characteristic benign tumor. There were no palpable glands in any part of the body and no pigmentation in any part of the skin, although she had had a pigmented pedunculated wart in this region of her body for a great many years. The growth was removed by Dr. Nassau under cocaine. She came back in two months with enlarged glands in her right axilla and three darkly pigmented bodies on the skin near the scar of the primary operation. These glands were excised and they proved to be metastases from a melanotic sarcoma. Later the supraclavicular glands enlarged and were removed, and also showed metastases within two weeks. After the removal of these glands in the neck and axilla metastases appeared in the skin all over the body. This has been the second observation that we have made in the hospital of the sudden appearance of these nodules. The interesting features of the case were the benign appearance of the primary tumor, with no evidence of its infiltration through the pedicle into the axilla, and the sudden appearance of the metastases.

Dr. BLUMER.—The autopsy was made over 48 hours after the patient's death, so that the body was not perfectly fresh. There were, however, no marked signs of decomposition. The site of the operation in the upper part of the chest was fairly clear, but in the axilla extending to and involving the right breast was a solid mass of new growth which in spots showed pigmentation. This mass was about the size of a fist. The surface of the body, particularly of the chest and abdomen, was covered with small nodules, varying in size from that of a pea to that of a large bean. Some of them were attached to the skin, others were not. Some were pigmented, some were not. None of them were very darkly pigmented, the pigmented ones being rather light brown in color. There were very few metastases in the skin over the back and extremities; none, if I remember correctly, on the arms and legs. On cutting into the abdominal muscles they were also found to contain small metastases, some pigmented, others non-pigmented. The muscles of the back likewise contained a large number of pigmented metastases. The peritoneal cavity contained a moderate quantity of fluid, and both layers of the peritoneum were studded with tumor metastases varying in size from a miliary tubercle to a large bean. The most marked metastases in the peritoneum were in the dependent parts, particularly in the pelvis, over the bladder and around the appendix. It seemed almost certain in this instance that these were metastases due to transplantation, that tumor cells had been free in the peritoneal cavity and had gravitated to the lowest part and become affixed there. The parietal layer of the pericardium contained no metastases, nor did the heart muscle itself. In the visceral layer of the pericardium were two or three pigmented metastases not larger than a pea. On the surface of both lungs just beneath the pleuræ were quite a large number of metastases, most of them small, and the substance of the lungs also contained similar ones. In all these situations the metastases varied both in size and color. The liver contained but a single metastasis, which was only found after prolonged search. The adrenals both contained small metastases, as did also the kidneys and spleen. There were no metastases in the bladder beyond those on the peritoneal surface. The uterus was also free as far as we could make out. In the right ovary was a nodule about the size of a pea. The intestines showed numerous metastases on the peritoneal surface, particularly along the mesenteric attachment, and a few metastases were present in the mucous membrane of the rectum, and in the mucosa here and there throughout the intestines. There were one or two small nodules in the pancreas. The thyroid gland was normal on the left side, but the right lobe was considerably enlarged and hemorrhagic. Outside the hemorrhagic area, which occupied the center, was quite a large area of tumor metastasis presenting the same character as the metastases elsewhere. The periosteum of one of the ribs, the 7th or 8th on the right side, and the pericranium in the right parietal region both contained small metastases. The one in the pericranium penetrated some distance into the parietal bone, but did not pass into the cranial cavity. The dura was entirely free, but there were numerous metastases in the pia-arachnoid, most of them of small size.

The brain showed a considerable number of metastases. They looked very much like small cysts with dark contents in the brain substance, but on cutting into them they were found to be pigmented metastases, and here the pigment showed up much better than in other parts of the body. A great many of the metastases were situated in the cortex. There were also

numerous metastases throughout the brain substance. There was one moderately large one in the right crus of the cerebrum and one of similar size in the right lobe of the cerebellum, and several scattered around and through the gray ganglia at the base.

The bacteriological examination simply developed the fact that the patient had a general staphylococcus infection, which was probably the immediate cause of death.

There are several points of interest in this case. In the first place the distribution of the metastases was of interest. The places in which metastases are rare and in which they occurred in this case are in the genital organs (right ovary), in the pancreas and in the thyroid gland. A most curious clinical feature is that notwithstanding the extensive involvement of the brain there were absolutely no signs of brain involvement during life. It was noted after death that the right pupil was much larger than the other.

An interesting feature of this class of tumors concerns the melanin which causes the coloration of the tumors, and the origin of this melanin. Does it come from the blood directly, or is it a product of cell activity? As far as I know there is nothing to prove that it comes from the blood. Iron has never, with possibly one exception, been found in the pigment, although this does not absolutely exclude a blood origin, as in malaria we know that the pigment, which does not contain iron, comes from the blood. It seems probable, however, that the pigment in these cases comes from some secretory activity of the cells themselves.

Another point of interest in these cases is the changes sometimes found in the urine—the so-called "melanuria." In the urine, sometimes immediately after voiding, sometimes not until later, there appears a dark pigment. Such urine is found to contain a substance called melanin, but it is not the melanin that gives the dark color to the urine, but some other substance excreted at the same time. The melanin has been isolated, but when tested does not give the reaction. The substance found in the urine is not present solely in melanuria, but also in cases where there is an excess of indol.

Specimen of Adeno-Carcinoma of Pancreas.—Dr. BLUMER.

This case came into the medical side with a diagnosis of brain tumor. The man had several symptoms of tumor of the brain, some inco-ordination and double choked disk, but no definite paralysis. On careful examination he was found to have a definite abdominal tumor in the median line suggesting an enlargement of the retroperitoneal glands. I do not know that a flat-footed diagnosis was made during life, but it was suggested that it was perhaps a primary tumor of the pancreas. The autopsy was made 24 hours after the death of the patient. He was much emaciated and jaundiced. There were no metastases to be made out externally. On opening the abdomen the liver was found much enlarged, and there was a very large mass occupying the median line in front of the spinal column, and a large mass in the left flank. The parietal peritoneum was free from metastases. The visceral peritoneum showed a few metastases over the intestines, and one rather interesting metastasis over the appendix vermiformis. This metastasis over the appendix had a circumference about that of a dime and had completely obliterated the cavity of the appendix. It had evidently grown in from the peritoneal side and pushed the walls of the appendix together, as the sections demonstrate.

The pericardium in this case showed metastases from a direct extension from the bronchial glands. The heart muscle was the seat of one metastasis, in the left ventricle. There were a large number of metastases on the pleuræ and in the substance of the lungs. The bronchial glands on the right side had grown directly into the right bronchus, and there were numerous tumor nodules projecting into this.

The liver weighed some ten or twelve pounds. It contained a very large number of metastases which were distinctly umbilicated and had all the characteristics of carcinoma metastases. The common bile duct was entirely obliterated, being included in the large mass which lay in front of the vertebral column. The gall bladder was very much dilated and extended a hand's breadth below the margin of the liver. The right adrenal gland was entirely replaced by a mass of tumor substance not very much larger than the normal adrenal. In the place of the left adrenal there was a tumor mass about the size of a fœtal head at term, and no sign of adrenal substance. This mass had grown directly into the left kidney, in which, beside this growth, there were a number of metastases about the size of a pea. There were similar small metastases in the right kidney. The spleen was free from metastases, as were the other organs, with the exception of the lymph glands and the cerebellum. The peripancreatic glands were very much enlarged and formed a mass the size of a cocoanut, which lay in front of the vertebral column. No trace of the pancreas could be found; it had been entirely replaced by the tumor mass. No trace of it could be found microscopically.

The meninges showed no metastases, nor did the cerebrum, but springing from the dura lining the right posterior fossa of the skull and compressing the right lobe of the cerebellum, there was a tumor about the size of a pigeon's egg. This did not directly compress anything beyond the cerebellum. This, of course, accounted for the cerebral symptoms which the man had during life.

It seems to me that the most interesting point in this case is the fact that both the pancreas and the adrenals were entirely thrown out of function without definite symptoms resulting therefrom. The man, as far as had been made out, had certainly had no symptoms of Addison's disease during life, and the urine had been free from sugar. Of course there have been a number of cases of Addison's disease reported in which there was absolutely no disease of the adrenals, and, again, there have been cases of total destruction of the adrenals in which there were no symptoms of Addison's disease. There have likewise been cases of entire replacing of the pancreas with new growth without any diabetic symptoms. The question arises whether or not the tumor cells arising from these different organs can take on any of the functions of the organ from which they grow, whether they can keep up the so-called internal secretion of the organs which is necessary for the preservation of health. The microscopical appearance of the tumor suggests that it came from the pancreas. It is an adeno-carcinoma. According to the present understanding of

metastasis, the cells of the tumor occurring in the adrenal should have taken on the character of pancreatic cells and not of adrenal cells, in which case the internal secretion of the adrenals would have been entirely lacking. The question whether in such a case the cells in the pancreatic tumor and in the adrenal tumor secrete the substance normal to the cells of each of these organs is one which needs further investigation.

Discussion.

Dr. Flexner.—The example of generalized melanotic sarcoma presented by Dr. Blumer has many points of interest. I wish to add a word regarding the pigments of these growths. It is at least probable that this pigment has the same origin as that present normally in the skin, hair, choroid coats of the eye and substantia nigra of the brain. Until the chemical nature of the normal pigments is more fully investigated and the melanin of this class of sarcomata obtained in a purer state than has been hitherto done, it will not be possible to state definitely what their relation is. We are comparatively well informed concerning the origin of certain of the pathological pigments, and indeed, although less fully, of their chemical composition. We find in given cases no difficulty in referring certain pathological pigments to the bile and others to the blood. Among those derived from the blood are at least several quite well characterized kinds which are yielded by the coloring matters of the red blood corpuscle—hæmatoidin, a definite chemical body hæmafuscin, less well defined, being devoid of iron; and hæmosiderin, a chemical complex which contains iron in a readily demonstrable form. The dark pigment found in the blood, organs and parasites themselves in malaria and to which the name "melanin" is also applied, differs chemically, according to Carbone, from the pigment of melanotic sarcomata.

The pigment in these tumors is deposited in smaller part within the tumor cells than in the interstitial framework of the growths. Where the quantity of coloring matter within the tumor cells becomes considerable the cells tend to degenerate, and thus it happens that areas occur which apparently consist of pigment only. The color of the latter varies considerably, and in certain tumors or in some metastases of otherwise dark tumors it is of a light brown or almost yellow color. So far as we are informed at present the pigment is produced—autochthonously, if you please, by the tumor. However, other views have prevailed at different times. Schmidt has drawn attention to the circumstances that a small portion of the pigment in nearly all melanotic sarcomata gives the reaction for iron, that the pigment is present in the connective tissue septa as well as in the tumor cells, that, further, at times there is considerable pigmentation of organs at a distance from the tumors, and he has used these facts to support the idea that the pigment may be formed elsewhere, and after partial loss of the iron reaction be transported to and deposited within the tumor. He thinks that he has found additional support in the observations of Wagner of the existence of masses of pigment in the heart and kidneys independent of tumor formation in cases of melanotic sarcoma of the skin associated with numerous actual metastases, and of Oppenheimer, who noted in melanotic skin sarcoma discoloration and pigmentation of the skin, mucous membranes, serous membranes and adipose tissues. A more probable explanation of the iron-containing pigment is that it is derived directly from the transformation of the hæmoglobin of the red blood corpuscles, as actual hemorrhages are not uncommon in these tumors.

The chemical analyses of the dark pigment (melanin) have yielded results somewhat at variance with one another. Iron has been detected in it (Eiselt, Nencki-Oppenheimer, Mörner, Dressler) by some and missed by others (Virchow, Berdez, Nencki). Hence the question of a direct blood origin of the pigment is more or less still a disputed one. An interesting observation has been made by Berdez and Nencki and by Mörner, who found in melanin a large percentage of sulphur, in some instances exceeding 10 per cent. Even this observation has been variously interpreted as proving and as disproving on the one hand origin from the blood, and on the other autochthonous formation. Finally Joos has conceived that the sarcoma cells produce the pigment from the colorless albuminous bodies of the blood plasma. The conclusions which have been arrived at by Abel and Davis (The Journal of Experimental Medicine, 1896, Vol. I., No. 3) in their painstaking study of the pigment of the negro's skin and hair are as follows: The pigment isolated from the containing granules contains only the merest trace of iron—so little, in fact, that it must be considered when entirely pure as free of iron. They further conclude, from the results of their work, that the pigment is not a derivative of hæmoglobin, but probably is ultimately derived from the proteids of the parenchymatous juices.

NOTES ON NEW BOOKS.

Ueber die Beziehungen der Leucocyten zur Bactericiden Wirkung des Blutes. By Martin Hahn, Assistant at the Hygienic Institute at Munich. Munich, 1895, Oldenbourg, pp. 1–42.

In this monograph of Dr. Hahn's presented to the K. Ludwig-Maximilian University, *pro venia legendi*, a series of investigations are reported regarding the relations of the leucocytes to the bactericidal action of the blood. The article opens with a discussion of previous work on the same subject. The objections made by Metschnikoff to the views advanced by Hankin and Kanthack are considered, and the researches of Denys and Havet, and of Vaughan and McClintock, are referred to. Hahn's work follows directly upon some experiments previously made by Buchner. He injected *Aleuronatbrei* into the pleural cavity of rabbits and obtained from them after 24 hours, blood serum and defibrinated blood, as well as the pleural exudate. The latter was frozen and quantitative bactericidal experiments made with it. He found like Schuster that the exudate rich in leucocytes far exceeds the serum in bactericidal activity, due to the increased amount of labile bodies present in it, bodies which probably have their origin in the leucocytes. He made further experiments with isolated leucocytes, proving that the addition of a salt-solution extract of leucocytes to ordinary blood serum definitely increases its bactericidal powers. An interesting exception to this rule was the fact that cholera bacteria appear to resist markedly the action of leucocyte fluid obtained by means of *Aleuronatbrei*. This the investigator attributes to two causes: (1) the presence of small amounts of aleuronatbrei diminishes the bactericidal power of the serum, and (2) the

serum after the destruction of the alexines is not favorable for the development of comma bacilli.

Further experiments were made with histon blood with the object of determining whether the bactericidal activities depend upon decomposition products or upon actual secreting products of the leucocytes. In histon blood, in contradistinction to defibrinated and coagulated blood, the leucocytes are preserved in good condition, and it was found that in it or its plasma the same bactericidal activity was developed as is characteristic of the defibrinated blood or serum of the same animal. Phagocytosis was excluded inasmuch as the plasma, freed from cells, was just as active as the blood containing leucocytes. Hahn concludes, therefore, that the bactericidal activity of the serum does not depend upon products resulting from the destruction of the leucocytes, but much more upon substances representing actual secretions of these cells. The article closes with some interesting considerations upon the relation of the substances under consideration to natural immunity and to therapy, and some emphasis is laid upon the possibility of increasing them artificially within the body. Those interested in this field of investigation will be well repaid by a perusal of the original article. L. F. B.

DIABETES MELLITUS.*

This work of Dr. Weintraud's has its special interest, not so much from any light it throws on the real local disturbance in diabetes, as from its dietetic point of view, and the interesting problems it brings up in relation to the processes of digestion in this disease. The value of the fats in the nourishment of diabetic patients is especially considered, the extent of their absorption, their influence on the destruction of albuminoids and on the excretion of sugar. The author proves that patients who have diabetes, but who are for the time being passing no sugar in their urine, may be kept in a state both of nitrogenous and body weight equilibrium, with the same amount of albumens and fats as a healthy person, and that they do not need a food which represents a higher caloric value than that required by a normal individual. He shows that from 200 to 300 grammes of fat can be eaten daily by patients with diabetes, and that this amount of fat is well borne, and that even with a diet consisting of 78 per cent. of fat the nitrogenous equilibrium of the body is well maintained.

Vogt's theory that the metabolic processes in diabetes are not diminished by any means, but rather increased, is thus substantiated.

There is, as has long been known, an increase in the nitrogen excreted in diabetes. Further, in order to keep up a nitrogenous equilibrium on a diet consisting largely of albuminoids, there must be an increased destruction of them, dependent on certain changes of the destroying cells and tissues. It has been thought by some physiologists that this increased destruction of the albuminoids represents a peculiar metabolic disturbance in diabetes; but in Vogt's laboratory it has been shown that the destruction of albuminoids occurring in patients with diabetes is not different from that in healthy men of like weight, when their food was free from carbohydrates. This leads Vogt to think that the quantitative changes in the metabolism of diabetes are not alone due to the presence of sugar, but also to the increased destruction of albuminoids. The presence of sugar is due to the fact that it is incompletely consumed by the organism, as a result of some true disturbance of function, and not to any diminution in the amount of oxygen taken in, for this in itself is merely secondary to the real disturbance. We know, moreover, that in diabetes the oxidation processes are not deleteriously influenced, for to consume fat is no easier than to consume carbohydrates.

The body heat is maintained, when the carbohydrates are eliminated from the food, by an increased destruction of corresponding quantities of fat and albumens, and Dr. Weintraud proves that in his cases only the same amount of albuminoids and fats was required as would have been required by healthy individuals of like weight living under similar conditions, to maintain both a nitrogenous and body-weight equilibrium. His theory is that the excretion of sugar is due to failure of the fermentative breaking up of the sugar molecule which is necessary before it can be attacked by oxygen. The enormous excretion of urea in diabetes shows that the breaking up and oxidizing of the albuminoids goes on in the ordinary way, and this is also true of the fats. In diabetes the source of heat is mainly the combustion of the fats, whereas in health the carbohydrates being much more easily oxidized, the heat is chiefly derived from their combustion. Such are a few of the points which come under consideration in the first half of the article.

The author then proceeds to take up the question of the value of fats. He shows that in almost all his experiments the fat has been absorbed in a completely satisfactory way. It has been experimentally proved that when the pancreas is extirpated, unemulsionized fats are not absorbed, and emulsionized ones in but sligh degree. But fat does not always occur in the stools of patients who have pancreatic disease, and Lancereux, describing certain cases of diabetes mellitus, as "diabète maigre," which he attributes to disease of the pancreas, says that in these cases the absorption of the albuminoid constituents of the food was not in any appreciable way modified by the addition of large masses of fat to the nourishment. That the consumption of fats actually does work to the advantage of keeping up the nitrogenous equilibrium in healthy individuals has been proved by other investigators, and Dr. Weintraud shows that this is also true in certain cases of diabetes, though at first, if the amount of the albuminoids ingested is large, there may be an increase in the excretion of nitrogen in the urine, but this condition does not last long and soon the nitrogenous equilibrium is restored. As yet there is no satisfactory explanation for this reaction. As regards the comparative value of fats and carbohydrates in saving the expenditure of albuminoids, all that need be said is that a given quantity of carbohydrates represents a higher caloric value than a like quantity of fats, but all that it is necessary to do is to give such a quantity of fats as would equal the caloric value of a given quantity of carbohydrates and in this way we could accomplish the same end, the saving of albuminoids, equally well.

In considering the question of the influence of fats on the excretion of sugar the author proves that no excretion of sugar, worthy of mention, is ever caused through increase of the fats in the food. At times small quantities of sugar are excreted, when change is made from a diet poor in fats to one rich in fats, but this increase is merely temporary.

The next point of interest which comes under discussion is whether Seegin's theory that sugar is formed in the liver from fat and albumen is correct, and Dr. Weintraud thinks not. He does not believe that in diabetes mellitus, where it is impossible to use up the sugar, an increase in fatty food would necessarily be followed by an increase in the production of the sugar, whereas on the other hand the introduction of albuminoids always leads to an increase in the excretion of sugar. Diabetic patients show an apparently unlimited tolerance towards fat, and Dr. Weintraud's experiments show conclusively that there was less sugar excreted when more fat was taken, which means that the destruction of the albuminoids was not so active as under other conditions, a fact which also opposes Seegin's theory. In Dr. Weintraud's cases an increase in the amount of sugar in the urine, after an increased diet of fats, was seen only in those experiments where there was apparently an increased destruction of albuminoids; such quantities of sugar as did appear in these experiments when

*Bibliotheca medica: D. H. Dr. Wilhelm Weintraud: Untersuchungen über den Stoffwechsel in Diabetes mellitus und zur diätetischen Therapie der Krankheit. 1898. Verlag von Th. G. Fischer & Co., Cassel.

the diet of fats was very large, were so small that they could not be estimated quantitatively, and were never in proportion to the amount of fats given. Had they been larger it might be possible to explain their appearance on the theory that in the combustion of the fats all the oxygen from the blood was used up, and therefore the combustion of the sugar was prevented, but under the circumstances this theory is hardly tenable. It is, however, on this ground that Lichtheim opposes a diet rich in fats, but in his cases the appearance of sugar in the urine may have been due to the large amount of albuminoids consumed. It is with this discussion of the place of fats in the diet of diabetes that the article practically ends, though there are a page or two on what may be called the dietetics of individual symptoms which may appear in the course of the disease. RUPERT NORTON.

A Manual of Syphilis and the Venereal Diseases. By JAMES NEVINS HYDE, A. M., M. D., Professor of Skin and Venereal Diseases, Rush Medical College, etc., Chicago, and FRANK H. MONTGOMERY, M. D., Lecturer on Dermatology and Genito-urinary Diseases, and Chief Assistant to the Clinic for Skin and Venereal Diseases, Rush Medical College, etc. With forty-four illustrations in the text and eight full-page plates in colors and tints. (*Philadelphia: W. B. Saunders*, 1895. Pp. 8-17 to 618. Price $2.50.)

In preparing this manual the authors have kept in mind the needs of the student and of the general practitioner, hence all matters of controversy have been subordinated to matters of fact.

The book treats of the diseases commonly classed as venereal, viz., syphilis, chancroid and gonorrhœa, and of a few minor affections to which the sexual organs are subject but not necessarily of a venereal origin. The text is illustrated by a few drawings, plates and photographs. Nearly one-half of the book is devoted to a description of syphilis. It is to be noted that a departure has been made from the usual custom of dividing this disease into primary, secondary, and tertiary stages, which are more or less artificial. The division rests upon clinical types, which are arranged according to the severity of the constitutional involvement, into four well-marked classes: 1. Benignant syphilis with mild and transitory symptoms; 2. Benignant syphilis with relapsing or persistent symptoms; 3. Malignant syphilis with relapsing or persistent profound symptoms; 4. Malignant syphilis with relapsing or profound lesions that are ultimately destructive.

The descriptions are given in a clear and entertaining style, and the definitions are exact and comprehensive. One is well repaid in glancing over the pages of this book, for the matter, although condensed, covers the field of venereal diseases completely.

J. W. L.

Obstetric Accidents, Emergencies and Operations. By L. CH. BRISLINIERE, M. D., LL. D. 8vo, pp. 381. Profusely illustrated. (*Philadelphia*, 1896, *W. B. Saunders.*)

This well-printed book is not a treatise on midwifery nor a manual of obstetrics, but is intended for the use of the practitioner when thrown upon his own resources and unable to consult more elaborate treatises upon midwifery. The style is clear and forcible and the directions given are judicious and well considered. It can be commended to those who desire a practical handbook to help them meet pressing emergencies.

A Manual of Anatomy. By IRVING S. HAYNES, Ph. B., M. D., Adjunct Professor of Anatomy, New York University. Pp. 680. 134 half-tone illustrations and 42 diagrams. (*Philadelphia*, 1896. *W. B. Saunders, Publisher.*)

This manual, which is more one of dissection than of general anatomy, as its title would seem to imply, is an example of careful study and thorough work. The illustrations are for the most part original with the author and in many instances are reproductions of photographs made from careful dissections; some are good; more are blurred and lacking accurate definition, probably owing to hopeless defects in the original photographs. The author's plan of reproducing actual dissections is worthy of much praise, and it is to be regretted that the negatives were not more carefully taken. Many of the diagrams illustrating the text are printed in two colors and are admirable aids to the text. The index is carefully compiled, and access to the vast amount of technical knowledge contained in the book is readily afforded by it. The book should be in the hands of surgeons and students of anatomy.

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